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CONTENTS

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ULTRASONIC DOPPLER CARDIOGRAPHY AS A METHOD OF STUDYING INFLIGHT CARDIODYNAMICS (RESULTS OF PATENT AND INFORMATION ANALYSIS)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 23 Apr 82) pp 4-8

[Article by V. S. Bednenko and A. N. Kozlov]

[English abstract from source] This paper reviews patent and information data on the methods of cardiac location using ultrasound dopplercardiography, as well as on the design and development of onboard equipment to be used for medical monitoring of aircraft and spacecraft crewmembers inflight. It is emphasized that dopplercardiography, being a very informative, noise-proof and relatively simple technique, holds high promise for operational medical monitoring.

[Text] Ultrasonic methods of studying cardiodynamics have gained popularity in medical monitoring systems for pilots and cosmonauts [1-3]. Use of the method of ultrasonic Doppler cardiography (USDC), which permits recording cardiodynamic parameters without the participation of an operator-physician [4, 5] is considered promising for systems of operational medical monitoring (OMM). The equipment for USDC has some substantial advantages over echocardiography with regard to its size and weight [6, 7]. It can be used to transmit information via telemetry systems with minimal interrogation [4, 8]. However, there are still no standard approaches to choice of methodological procedures and execution of measuring channels of doppler cardiography. We submit here the results of a patent and information analysis of methodological procedures and use of USDC for examination of cardiodynamics.

USDC is based on probing the heart with ultrasonic waves of low intensity in modes of continuous monochromatic radiation and reception, by means of comparing the emitted reference wave to the signal reflected from a moving part of the cardiac structures. Information about the functional state of the heart is contained in changes in shape and amplitude-frequency characteristics of reflected signals [4, 5, 9]. The dynamics of duration of Doppler cardiogram complexes reflect changes in phase structure of the cardiac cycle [5, 10, 11]. The frequency of the signals is proportional to the velocity of cardiac elements in accordance with the Doppler effect [12, 13], whereas variations of its level are proportional to the dynamics of the myocardium's elastoplastic properties [14].

As applied to OMM, a "nonsearch" method was developed for USDC recording, in which the sensor of ultrasonic waves is placed in the probing zone by means of an elastic belt [15]. In order to increase the reliability of registration, we developed a system that provides for additional tightening of the belt and use of molded liners [16]. For "nonsearching" USDC, a topographic map was plotted of the zones of the heart and great vessels [5].

The zone of most stable probing by the Doppler cardiographic method is in the region of the 3d-6th intercostal spaces, mainly to the left of the sternum [4, 5]. It is limited for OMM to the 5th-6th intercostal space along the parasternal line, since changes in position of the heart in this region are the least marked under the effect of flight factors [1].

The complete set of USDC signals per cardiac cycle is characterized by the presence of specific components (groups of oscillations or surges of different levels and filling frequencies separated by aphonic segments--pauses) reflecting the dynamics of the probed segment of the heart. These features were given an interpretation previously [5]. The anterior and posterior walls of the ventricles, interventricular septum, elements of the valve system are involved in forming the Doppler cardiogram, and in the overall corrected spectrum of the signal one can single out segments corresponding to each of these structures of the heart [17, 18]. However, since it is difficult, as yet, to make a complete spectral analysis with use of instrumentation, in OMM systems one singles out by means of a solitary filter the signals that reflect mainly the movement of the posterior wall of the left ventricle [1]. As shown by the results of the studies of V. V. Zaretskiy et al. [8], McDonald et al. [19], the dynamics of this cardiac element reflects the most fully the functional state of the myocardium.

The natural vibrations of the chest, which are marked during flights, affect only formation of the low-frequency range of the spectrum, and they do not hinder analysis of motion of the posterior wall of the left ventricle [20]. The probability of picking up ultrasonic signals reflected from the epicardium and endocardium is substantially higher, according to our studies, than from the pericardium.

These circumstances are the reason for the high noise-proof features and reproducibility of the method in OMM systems.

The equipment for USDC in current use under such conditions consists of the following elements: sensor part, amplifier-transformer circuit for high and low frequencies, system for processing and analyzing signals [4, 6, 9]. The ultrasonic sensors are executed in the form of a receiving-transmitting transformer of acoustic waves consisting of two half-discs contained in the same housing [21]. The amplifier-transformer circuit is based on direct transformation of signals. The processing system has three channels: channel for isolating the Doppler beats (direct signal) from the USDC, amplitude detection channel (to single out the envelope level of the Doppler cardiogram) and frequency detection channel (to select a signal proportional to velocity of movement of cardiac elements). In order to obtain integral values for the above parameters, we use specialized devices that store the parameters, either for the duration of cardiac cycles or discrete intervals [22, 23]. The integral values can be calculated by means of a computer using specialized

programs for data processing [24, 25], which is important when processing large arrays of information. Frequency analyzers of the series and parallel types, with display of the signal in the form of corrected spectra [17, 26] are used for analysis of propulsive activity of intracardiac structures.

Table 1. Informativeness of USDC and features used to calculate cardiodynamic parameters

Informative capability of USDC	Informative features used in calculations	Author, source
Determination of heart rate	Number of contraction cycles	A. N. Kozlov [28], Grote [29], Boldner [30]
Determination of phase structure of cardiac cycle	Amplitude and frequency characteristics of USDC complexes	A. N. Kozlov et al. [5], V. A. Degtyarev et al. [15]
Determination of dynamics of cardiac output	Integral frequency parameters of signal in sphygmic phase	V. S. Bednenko et al. [31], V. A. Degtyarev et al. [32]
Evaluation of dynamics of effective coronary blood flow	Integral values of amplitude parameters of signal in systole	V. S. Bednenko et al. [33-35]
Measurement of velocity of cardiac elements	Frequency parameters of USDC. Frequency of corrected spectrum maximums	A. N. Kozlov et al. [17], Abelson et al. [12]
Determination of energy relations between contractility of myocardium of anterior and posterior walls of left ventricle in systolic and diastolic phases	Intensity of maximums of overall corrected USDC spectrum	A. N. Kozlov et al. [17]

In addition the instruments for USDC have an audio monitoring unit, which is necessary to pinpoint the probed zone as related to individual anatomical distinctions of subjects [4, 9].

The main parameters of instruments for Doppler cardiography are: intensity of ultrasonic waves (I), ultrasound carrier frequency (f), coefficient of system amplification (K) and magnitude of Dopplerian frequency shift (F). The values of these parameters should constitute: $I \leq 0.05$ W/cm^2, f = (2-3) MHz, K = (60-80) dB and F = (150-750) Hz [27].

The informativeness of USDC, as well as features used to calculate cardiodynamic parameters, are listed in Table 1.

The Doppler cardiography method permits determination of heart rate, complete phase analysis of cardiac function (including diastolic phase), dynamics of

expulsion of blood and efficiency of coronary blood flow. In addition, it permits evaluation of velocity of cardiac structures and energy relationships of myocardial contractility in systole and diastole. Determination of dynamics of stroke volume is based on discrimination of Doppler signals reflected from the posterior wall of the left ventricle. Evaluation of dynamics of efficient coronary blood flow is based on the experimentally determined integral values of reflected signal in systole as a linear function of blood volume in the coronary channel, which are related by the dynamics of contraction of myocardial myofibrils.

Table 2. Future directions of refinement of USDC method and equipment, according to analysis of patent data

Upgrading construction principle	Expected effect	Author, source
Addition of second ultrasound channel	Increased accuracy in speed measurement, detection of direction of motion of cardiac elements	V.V. Besschetnikov et al. [41], Hatke [42]
Addition of EKG and pneumography channels	More accurate measurement of cardiac cycle phases	A. N. Kozlov et al. [43]
Use of multi-element sensors	Increased reliability and stability of picking up USDC signals	V. L. Kuznetsova [44], Goldberg [45], Zandley [46], Phillips [47]
Addition of airtight water containers to provide acoustic contact between sensor and body	Possibility of recording USDC without removal of pilot's gear	D. M. Murdock [48], Budde [49]
Use of additional parallel channels for signal frequency processing	Synchronous recording of dynamics of several cardiac elements	V. M. Lube et al.[50], A. N. Kozlov et al. [17], Freeman et al. [13]
Use of circuits for intermediate transformation of USDC signal spectrum	Possibility of using radiotelemetry systems to relay information with minimal interrogation	A. N. Kozlov [4]

Actual experience with USDC in OMM systems aboard aircraft of transport aviation made it possible to demonstrate the hemodynamic reactions of transport aviation pilots at different phases of flight [1]. Under these conditions, there was substantial increase in stroke volume (by 1.5 times) during landing, with increase in minute volume when making landing approaches (by 1.5 times) and landing (2 times). The changes in phase structure of the systole were moderate in horizontal flight and landing approaches, but there was substantial shortening of the sphygmic phase during landings. The phase structure of the diastole also underwent substantial changes during landing and, in a number of instances, landing approaches (shorter intervals of isometric ventricular relaxation, rapid and slow filling).

Dynamic inflight monitoring of these parameters could furnish additional information for setting standards for flight work, since it is possible to detect functional hemodynamic changes, as well as early stages of cardiac insufficiency [36-38] on the basis of deviations of these parameters during work loads and functional tests, as indicated by clinical studies.

The velocity of movement of the myocardium, as determined by USDC, is an additional informative feature in detecting cardiac insufficiency, since a specific change in velocity, primarily a decline, is inherent in various forms of cardiac pathology [39, 40]. The parameters of energy correlations between myocardial contractility in systole and diastole are also reliable diminished in the presence of disturbance in myocardial contractile function [17].

Analysis of the patent literature enabled us to single out future [or promising] directions for upgrading USDC methodology and equipment, which are listed in Table 2.

They involve the use of several transmitting or receiving channels and multi-element sensors, use of channels for synchronizing signal processing by means of other physiological parameters, use of multichannel processing systems, as well as intermediate transformation of Doppler cardiograms. As a result of their use, reliability and stability are improved with regard to picking up USDC signals, measurement of recorded parameters will be more accurate, the informativeness of Doppler cardiograms will be expanded, and it will be possible to relay information via telemetry systems with minimal interrogation. The practical execution of the above-listed methods of improvement will impart to the USDC method additional capabilities with regard to evaluation of contractile function of the myocardium.

The above-mentioned informativeness, rather high imperviousness to noise and relatively simple technical execution warrant consideration of the USDC method as promising for inflight OMM systems.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 629.78.612.015.6

VITAMIN LEVELS IN COSMONAUTS IN PREFLIGHT TRAINING PERIOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 1 Mar 82) pp 8-10

[Article by M. S. Belakovskiy, N. D. Radchenko, N. G. Bogdanov and V. B. Spirichev]

[English abstract from source] Measurement of vitamin supply of cosmonauts during their intensive training a month preflight showed moderate deficiency of thiamine, riboflavine, pyridoxine, nicotinamide and ascorbic acid. A regular uptake of the vitamin complex for 2 weeks optimized significantly vitamin metabolism.

[Text] Several authors have established that extreme states are associated with increased utilization of vitamins, impaired metabolism of vitamins and, consequently, differentiated change in requirements. The results of some studies indicate that there is a change in vitamin metabolism and utilization in the presence of adaption stress during air and space flights [1-3]. Analysis of metabolic reactions that implement processes of adaptation to spaceflight factors shows that vitamins and their metabolites play an important part in these reactions, maintenance of physical, as well as mental work capacity of man, and his health as a whole. For this reason, investigation of vitamin levels in cosmonauts during the period of intensive training for spaceflights is of considerable interest.

Methods

We assayed the concentrations of vitamins and their metabolites in venous blood and 24-h urine, coenzyme forms contained in blood, which include vitamins, and we studied some vitamin-dependent reactions. One month before flight, we assayed the concentration of retinol, cyanocobalamin, carotenoids, ascorbic acid, α-tocopherol, active transport form of vitamin D_3-25-hydroxycholecalciferol (25-OH-D_3), thiamin diphosphate effect (TDPE), transketolase activity of erythrocytes (TKAE), flavin-adenine-dinucleotide effect (FADE) determined by glutathione reductase (GR) activity with and without addition to reaction mixture of flavine-adenine dinucleotide (FAD), total nicotinamide (NAD+NADP) coenzymes [4-10] in venous blood taken on a fasting stomach. We assayed thiamin, riboflavin, N_1-methylnicotinamide (metabolite of vitamin PP), 4-pyridoxic acid (metabolite of vitamin B_6) and ascorbic acid in 24-h urine collected in the same period, as well as 1-7 days before flight [11-15]. The cosmonauts were kept on a controlled diet throughout the period of this study.

Results and Discussion

The results of our studies of parameters of vitamin metabolism, which were conducted during the period of intensive training 1 month prior to a spaceflight (Tables 1 and 2), led us to conclude that their mean levels conformed to the conventional standard for healthy men. At the same time, there were comparatively wider fluctuations of some parameters of vitamin metabolism. This is apparently related both to individual metabolic distinctions and some differences in diet, physical and mental loads. It must be noted that we observed some vitamin deficiencies during this period. For example, in 23% of the cases, the level of thiamin excretion in urine was slightly less than 150 μg/day, i.e., below the bottom range of the physiological norm. We demonstrated a decline of TKAE and relatively high TDPE. The coefficient of activation of GR of erythrocytes, as determined with addition of its coenzyme FAD, exceeded 1.2 in 15.2% of the cases, which was indicative of some riboflavin deficiency. Analogous findings were made in our examination of riboflavin excretion in 24-h urine. In some cases, there was a decline in excretion of 4-pyridoxic acid, N_1-methylnicotinamide and ascorbic acid, the levels of which did not reach normal values. A moderate vitamin A deficiency was found in 20.3% of the tested specimens, carotenoid deficiency in 3.1%, vitamin B_{12} deficiency in 3.1% and ascorbic acid deficiency in 22.6%. The concentrations of vitamin E and 25-OH-D_3 were never below the physiological norm, in spite of the relatively large number of tests (57 and 43, respectively).

Table 1. Parameters of vitamin metabolism in cosmonaut blood 1 month before spaceflight

Parameter	Physiological norm	Mean data
Vitamin A, μg%	30-70	45.0±1.5
Carotenoids, μg%	80-230	156.6±5.6
Vitamin B_{12}, pg/mℓ	200-1000	742.9±55.7
Ascorbic acid, mg%	0.7-1.2	1.49±0.15
25-OH-D_3, ng/mℓ	10-100	51.7±2.7
Vitamin E, mg%	0.6-1.6	1.56±0.05
TDPE, %	0-15	13.9±1.5
FADE, absolute units	<1.2	1.08±0.03
NAD + NADP, μg/mℓ	28.0-44.0	28.0±1.8

Considering the high level of physical and mental loads during the training period for a spaceflight, as well as the impending effect on cosmonauts of the set of combined extreme flight factors, preventive intake of a complex consisting of the following vitamins was recommended for all cosmonauts, for 2 weeks prior to the flight: retinol, thiamin, riboflavin, pyridoxine, folic acid, tocopherol acetate, methionine, cyanocobalamin, ascorbic acid and nicotinamide. Recheck urinalysis 1-7 days before the flight was indicative of appreciable increase in concentration of the following components in 24-h urine: thiamin by 77.9%, riboflavin by 29.3%, 4-pyridoxic acid by 95.1%, N_1-methylnicotinamide by 40.9% and ascorbic acid by 132.4%. Parameters of vitamin metabolism in blood were not examined at this time.

Table 2. Daily excretion in urine of vitamins and metabolites during preflight cosmonaut training

Parameter	Physiol. norm	1 mo preflight	1-7 days preflight
Thiamin, μg	150-500	336.8±16.8	599.1±49.6
Riboflavin, μg	300-1000	478.8±31.0	619.3±52.5
4-Pyridoxic acid, mg	1.5-2.5	2.25±0.13	4.39±0.23
N_1-methylnicotinamide, mg	7-1.2	9.39±0.34	13.23±0.52
Ascorbic acid, mg	20-30	25.0±4.4	58.1±5.7

Our results are indicative of a need for regular checking of cosmonauts' vitamin supply during the period of their flight training. Preventive intake of vitamins during this period should be instrumental in obtaining a high vitamin level in their system.

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EFFECT OF LONG-TERM SPACEFLIGHTS ON HUMAN AMINO ACID METABOLISM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 23 Apr 82) pp 10-15

[Article by A. S. Ushakov, T. F. Vlasova, Ye. B. Miroshnikova, V. M. Mikhaylov and Ye. N. Biryukov]

[English abstract from source] The amino acid composition of the plasma and serum of Salyut-6 crewmembers who performed flights of different duration was investigated. The parameter was found to vary depending on the flight time and use of different countermeasures. The 75- and 185-day cosmonauts who did not exercise in a full measure showed a decrease in the amino acid pool typical of emergency situations. The 96-, 140- and 175-day crewmembers who exercised as prescribed exhibited the lack of changes in the total content of amino acids and variations in the content of individual amino acids. The results of the study of the amino acid composition can be applied to the evaluation of inflight countermeasures, e. g. exercises, and to the development of rehabilitation measures postflight.

[Text] The set of spaceflight factors has a diversified effect on metabolic processes, particularly protein metabolism. Amino acids, which hold a key place in protein metabolism, are actively involved in numerous reactions of intermediate metabolism and synthesis of various biologically active substances. All this caused interest in studying amino acid metabolism as related to adaptation processes and determining its mechanisms under the extreme conditions of spaceflights. With regard to amino acid metabolism, it is of greatest interest to investigate blood plasma amino acid levels as one of the possible criteria in medical monitoring under extreme conditions.

For this reason, we are reporting here on a study of free amino acid content of peripheral blood plasma in main expedition crew members (MEC), who participated in missions differing in duration aboard the Salyut-6 orbital station: 96 days (MEC-1), 140 days (MEC-2), 175 days (MEC-3), 185 days (MEC-4) and 75 days(MEC-5).

Methods

In all instances, free amino acid concentration was assayed in blood plasma or serum taken from the ulnar vein at different preflight times, as well as 1st and 8th postflight days; in the case of MEC-1, we took samples on the 1st and 33d days. Amino acids were assayed on automatic analyzers using the method of ion exchange chromatography [1, 2] with prior deproteinization of specimens with sulfosalicylic acid [3]. The results were compared to individual free amino acid levels in blood plasma or serum assayed at different times during cosmonaut training, which were submitted to statistical processing.

Results and Discussion

Table 1 lists data from the literature concerning blood plasma and serum free amino acid content assayed for essentially healthy man [3-5] and separately for cosmonauts [4], taking into consideration the specifics and occupational activities of the intensive training period. Tables 1-3 list the results of studies of concentration levels of free amino acids in blood plasma and serum of MEC 1-5.

Analysis of the findings revealed that there was a decline in amino acid stock in blood serum of both crew members--commander (CDR) and flight engineer (FLE)--on the 1st day of readaptation to earth after a 75-day flight (MEC-5), which was more marked in the FLE. Overall free amino acid content on the 1st postflight day constituted 28.2 mg% in the CDR (32.1 mg% preflight) and 17.3 mg% in the FLE (37.7 mg%; see Table 1). While the decline of amino acid levels in the CDR was attributable essentially to decrease in concentrations of cystine (by 3.7 times), alanine (by 2 times) and tyrosine (by 3 times), in FLE there was a decline in levels of virtually all free amino acids of blood serum. There was no restoration of amino acid stock of the CDR on the 8th postflight day.

An increase in flight duration to 96 days (MEC-1) did not elicit appreciable changes in blood amino acids. Overall blood plasma amino acid levels were within the average physiological range; however, they were somewhat above preflight values, while individual decline and elevation of amino acids were also observed. Thus, on the first postflight day, alanine concentration increased by 0.7 and 1.9 times in the CDR and FLE, respectively. In addition, the CDR showed an increase (2-fold) in aspartic acid content, against a background of diminished concentration of glutamic acid (by about 1.3 times) and proline (1.4 times); in the FLE, there was an increase (2.3-fold) in threonine concentration and insignificant (1.3-fold) decrease in cystine content. It must be noted that blood plasma amino acid concentration was virtually unchanged on the 33d postflight day (see Table 2).

After completion of the 140-day mission (MEC-2), the individual deviations of blood plasma free amino acid levels did not have an appreciable effect on overall content. Nevertheless, the CDR presented elevation of blood plasma aspartic acid (2-fold), glutamic acid and phenylalanine (insignificant) and serine (1.7-fold) levels. The FLE showed changes in alanine content, whose level dropped by 2.4 times, as well as aspartic acid, whose level, on the contrary rose by 1.8 times. There was also an increase in concentration of tyrosine (1.4 times) and phenylalanine (1.6 times)(see Table 2).

Table 1. Blood serum free amino acid levels in MEC-5 (75-day flight) before and after mission

AMINO ACID	PHYSIOLOGICAL NORM, MG%					ACTUAL CONTENT, MG%					
	PLASMA			SERUM		CDR			FLE		
	DATA OF N. V. SEMENOV	OUR DATA [4] ORDINARY PEOPLE (n=80)	OUR DATA [4] COSMONAUTS (n=30)	DATA OF GERRISTEN [3]	OUR DATA FOR COSMONAUTS (n=10)	PREFLIGHT	POSTFLIGHT DAY 1	POSTFLIGHT DAY 8	PREFLIGHT	POSTFLIGHT DAY 1	POSTFLIGHT DAY 8
ISOLEUCINE	0,69—1,28	1,05±0,05	0,77±0,13	1,00	1,03±0,10	1,00	1,75 (+0,75)	0,58 (—0,32)	1,15	0,47 (—0,68)	2,08 (+0,93)
LEUCINE	1,42—2,30	2,03±0,08	1,48±0,10	2,3	2,09±0,11	2,35	3,25 (+1,20)	0,99 (—1,06)	2,33	1,19 (—1,14)	4,15 (+1,82)
VALINE	2,37—3,71	2,54±0,06	2,33±0,10	2,6	2,72±0,03	2,69	3,44 (+0,75)	1,17 (—1,52)	3,08	1,44 (—64)	2,20 (—0,88)
THREONINE	1,21+1,72	1,91±0,09	2,56±0,13	1,9	2,25±0,12	2,24	2,10 (—0,14)	1,17 (—1,07)	2,39	1,15 (—1,24)	1,73 (—0,66)
SERINE	1,05—1,25	2,02±0,09	1,34±0,07	2,5	2,95±0,99	5,05	4,17 (—0,88)	3,17 (—1,88)	3,80	4,35 (+0,55)	7,46 (+3,66)
METHIONINE	0,33—0,34	0,54±0,04	0,26±0,01	0,3	0,68±0,15	0,51	0,64 (—0,13)	0,41 (—0,10)	0,28	0,26 (—0,02)	0,82 (+0,54)
TYROSINE	0,69—0,95	1,04±0,06	0,80±0,05	1,4	0,93±20	1,74	0,51 (—1,21)	0,53 (—1,21)	1,57	0,84 (—0,73)	0,75 (—0,82)
PHENYL-ALANINE	0,82—1,43	1,13±0,06	0,73±0,04	1,9	1,60±0,15	1,60	1,51 (—0,09)	0,44 (—1,16)	1,25	0,96 (—0,29)	1,93 (+0,68)
CYSTINE	1,08—1,30***	0,91±0,10	0,73±0,04	1,5	2,76±0,30	2,96	0,80 (—2,16)	0,79 (—2,17)	2,90	0,47 (—0,43)	0,79 (—2,11)
ASPARTIC ACID	0,01—0,07	0,07±0,05	0,11±0,01	0,9*	1,10±0,05*	1,10*	1,18* (+0,08)	0,78* (—0,32)	1,46*	0,99* (—0,47)	2,17* (+0,71)
GLUTAMIC ACID	0,43—1,15	3,97±0,26	2,01±0,10	8,9**	4,39±1,00**	2,14**	1,80** (—0,34)	0,61** (—1,53)	3,87**	1,21** (—2,66)	2,45** (—1,42)
PROLINE	2,01—3,34	2,76±0,08	2,28±0,07	2,3	2,42±0,20	2,41	2,44 (+0,03)	2,79 (+0,38)	1,88	1,54 (—0,34)	4,57 (+2,69)
GLYCINE	1,34—1,73	2,32±0,09	1,32±0,09	3,1	2,35±0,18	2,27	2,50 (+0,23)	1,35 (—0,92)	1,78	1,14 (—0,64)	3,12 (+1,34)
ALANINE	3,01—3,73	3,80±0,14	2,44±0,10	4,3	4,36±0,15	4,29	2,15 (—2,14)	1,63 (—2,66)	4,99	1,31 (—3,68)	3,34 (—1,65)
TOTALS	16,5—24,4	26,1	19,2	34,9	31,6	32,1	28,2 (—3,9)	16,4 (—15,7)	37,7	17,3 (—20,4)	38,6 (+0,9)

Note: Here, in Tables 2 and 3 the deviations are indicated in parentheses.

*With asparagine **With glutamine ***With cysteine

Table 2. Blood plasma free amino acid levels in MEC-1 (96-day mission) and MEC-2 (140-day mission) before and after flight (mg%)

AMINO ACIDS	CDR (MEC-1) PRE-FLIGHT (n=4)	CDR (MEC-1) POSTFLIGHT DAY 1	CDR (MEC-1) POSTFLIGHT DAY 33	FLE (MEC-1) PRE-FLIGHT (n=4)	FLE (MEC-1) POSTFLIGHT DAY 1	FLE (MEC-1) POSTFLIGHT DAY 33	CDR (MEC-2) PRE-FLIGHT (n=4)	CDR (MEC-2) POSTFLT DAY 1	FLE (MEC-2) PRE-FLIGHT (n=4)	FLE (MEC-2) POSTFLIGHT DAY 1	FLE (MEC-2) POSTFLIGHT DAY 33
ISOLEUCINE	0,53±0,02	0,80 (10,27)	0,88 (−0,35)	0,56±0,22	0,81 (+0,25)	1,05 (+0,49)	0,68 ± 0,07	0,60 (−0,08)	0,73±0,07	0,73 (0)	0,69 (−0,04)
LEUCINE	1,03±0,09	1,93 (+0,09)	1,59 (−0,56)	1,16±0,16	0,81 (+0,55)	1,62 (+0,46)	1,27 ± 0,13	1,36 (+0,09)	1,09±0,03	1,43 (−0,34)	1,12 (+0,03)
VALINE	2,06±0,23	2,27 (+0,21)	2,22 (−0,16)	1,82±0,13	1,88 (+0,06)	2,41 (+0,59)	2,02 ± 0,22	2,14 (−0,12)	1,94±0,07	2,28 (+0,34)	2,13 (+0,19)
THREONINE	3,38±0,69	3,66 (+0,28)	4,53 (−1,18)	2,03±0,35	4,63 (+2,6)	3,61 (+1,58)	4,04 ± 0,40	4,36 (+0,32)	3,09±0,15	3,49 (+0,4)	3,10 (+0,01)
SERINE	1,45±0,21	1,43 (−0,02)	1,30 (−0,15)	1,28±0,12	1,53 (+0,25)	1,52 (+0,24)	0,94 ± 0,09	1,57 (+0,63)	1,22±0,10	1,25 (+0,03)	1,20 (−0,02)
METHIONINE	0,37±0,03	0,32 (−0,05)	0,34 (−0,03)	0,19±0,05	0,27 (+0,08)	0,32 (+0,13)	0,42 ± 0,02	0,30 (−0,12)	0,37±0,09	0,29 (−0,08)	0,30 (−0,07)
TYROSINE	0,58±0,10	0,97 (+0,39)	1,10 (−0,52)	0,61±0,04	0,95 (+0,34)	0,87 (+0,26)	0,70 ± 0,07	1,00 (+0,30)	0,58±0,02	0,82 (+0,24)	0,57 (−0,01)
PHENYLALAN.	0,50±0,02	0,94 (+0,44)	0,82 (+0,32)	0,63±0,07	0,93 (+0,3)	0,95 (+0,32)	0,64 ± 0,07	1,09 (+0,45)	0,50±0,05	0,82 (+0,32)	0,56 (+0,06)
CYSTINE	0,77±0,06	0,69 (−0,08)	0,50 (−0,27)	0,52±0,08	0,39 (−0,13)	0,53 (+0,01)	0,63 ± 0,11	0,59 (−0,04)	0,43±0,10	0,46 (+0,03)	0,64 (+0,21)
ASPART. ACID	0,09±0,02	0,19 (+0,1)	0,30 (+0,21)	0,11±0,05	0,16 (+0,05)	0,20 (+0,09)	0,13 ± 0,04	0,26 (+0,13)	0,08±0,01	0,14 (+0,06)	0,07 (−0,01)
GLUTAM. ACID	2,39±0,29	1,89 (−0,05)	1,45 (−0,94)	1,90±0,21	1,94 (+0,04)	2,44 (+0,54)	1,21 ± 0,09	1,70 (+1,49)	1,60±0,09	1,31 (−0,29)	1,25 (−0,35)
PROLINE	2,75±0,20	1,96 (−0,79)	2,08 (−0,67)	2,55±0,05	2,10 (−0,45)	2,38 (−0,17)	1,68 ± 0,10	2,23 (+0,55)	2,38±0,11	2,79 (+0,41)	2,46 (+0,08)
GLYCINE	1,37±0,24	1,87 (+0,5)	1,85 (+0,48)	1,46±0,09	1,77 (+0,31)	1,55 (+0,09)	1,62 ± 0,12	1,87 (−0,25)	1,23±0,21	1,24 (+0,01)	1,22 (−0,01)
ALANINE	2,65±0,15	3,73 (+1,08)	2,91 (+0,26)	2,57±0,14	4,95 (+2,38)	2,56 (−0,01)	2,23 ± 0,10	2,45 (+0,22)	2,92±0,38	1,24 (−1,68)	1,76 (−1,16)
TOTALS	19,9	22,7 (+2,8)	21,9 (+2,0)	17,4	24,0 (+6,6)	22,0 (+4,6)	18,1	21,5 (+3,4)	18,2	17,3 (−0,9)	17,1 (−1,1)

Table 3. Blood plasma free amino acid levels in MEC-3 (175-day mission) and MEC-4 (185-day mission) before and after flight (mg%)

AMINO ACID	CDR (MEC-3) PRE-FLT	CDR (MEC-3) POSTFLIGHT DAY 1	CDR (MEC-3) POSTFLIGHT DAY 8	FLE (MEC-3) PRE-FLIGHT (n=4)	FLE (MEC-3) POSTFLIGHT DAY 1	FLE (MEC-3) POSTFLIGHT DAY 8	CDR (MEC-4) PRE-FLT	CDR (MEC-4) POSTFLIGHT DAY 1	CDR (MEC-4) POSTFLIGHT DAY 8	FLE (MEC-4) PRE-FLIGHT (n=4)	FLE (MEC-4) POSTFLIGHT DAY 1	FLE (MEC-4) POSTFLIGHT DAY 8
ISOLEUCINE	0,47	0,39 (−0,08)	0,46 (−0,01)	0,56±0,06	0,81 (+0,25)	0,54 (−0,02)	0,55	0,55 (0)	0,44 (−0,11)	0,56±0,06	0,42 (−0,14)	0,95 (+0,39)
LEUCINE	0,92	0,89 (−0,03)	0,82 (−0,10)	1,43±0,06	1,69 (+0,26)	1,21 (−0,22)	1,11	1,07 (−0,04)	0,77 (−0,34)	1,43±0,06	0,70 (−0,75)	1,42 (−0,01)
VALINE	2,08	1,20 (−1,88)	1,21 (−0,87)	2,19±0,01	2,14 (−0,05)	1,85 (−0,34)	1,69	1,30 (−0,39)	1,48 (−0,21)	2,19±0,01	1,12 (−1,07)	2,64 (+0,45)
THREONINE	2,71	2,49 (−0,22)	2,82 (+0,11)	4,21±0,30	4,70 (+0,49)	3,66 (−0,55)	4,30	2,17 (−2,21)	1,75 (−2,55)	4,21±0,30	1,56 (−2,65)	1,79 (−2,51)
SERINE	0,79	0,93 (+0,14)	0,78 (−0,01)	1,90±0,29	1,32 (−0,58)	1,54 (−0,36)	1,58	0,91 (−0,67)	0,79 (−0,79)	1,90±0,29	0,53 (−1,37)	1,03 (−0,87)
METHIONINE	0,38	0,10 (−0,28)	0,15 (−0,23)	0,30±0,01	0,27 (−0,03)	0,32 (+0,02)	0,47	0,14 (−0,33)	0,26 (−0,21)	0,30±0,01	0,13 (−0,17)	0,34 (+0,04)
TYROSINE	0,78	0,51 (−0,27)	0,54 (−0,24)	0,71±0,05	0,99 (−0,28)	0,92 (−0,21)	0,55	0,71 (+0,61)	0,47 (−0,08)	0,71±0,05	0,45 (−0,26)	1,02 (+0,31)
PHENYLALAN.	0,54	0,41 (−0,13)	0,58 (−0,04)	0,60±0,03	0,80 (+0,20)	0,62 (+0,02)	0,49	0,81 (+0,3)	0,61 (+0,12)	0,60±0,03	0,44 (−0,16)	1,20 (+0,60)
CYSTINE	0,44	0,42 (−0,02)	0,36 (−0,08)	0,44±0,12	0,32 (+0,12)	0,40 (−0,04)	0,22	0,23 (+0,01)	0,22 (0)	0,44±0,12	0,20 (−0,24)	0,26 (−0,18)
ASPART. ACID	0,12	0,25 (+0,13)	0,24 (+0,12)	0,12±0,01	0,53 (+0,41)	0,16 (+0,04)	0,07	0,10 (+0,03)	0,07 (0)	0,12±0,01	0,07 (−0,05)	0,42 (+0,03)
GLUTAM. ACID	0,58	1,62 (−1,04)	0,98 (+0,40)	1,19±0,20	2,41 (+1,22)	1,34 (+0,15)	1,50	1,76 (+0,26)	1,78 (+0,28)	1,19±0,20	1,43 (+0,24)	3,61 (+2,42)
PROLINE	1,19	1,23 (−0,04)	1,18 (−0,01)	1,70±0,07	2,02 (+0,32)	1,15 (−0,55)	1,58	1,51 (−0,07)	1,60 (+0,02)	1,70±0,07	0,84 (−0,86)	1,99 (+0,29)
GLYCINE	0,75	0,97 (+0,22)	1,10 (+0,35)	1,19±0,08	1,67 (+0,48)	1,06 (−0,13)	1,21	1,09 (−0,13)	0,81 (−0,04)	1,19±0,08	0,70 (−0,49)	1,13 (−0,06)
ALANINE	1,89	2,19 (+0,3)	2,50 (+0,61)	2,15±0,12	3,69 (+1,54)	2,68 (+0,53)	2,09	2,13 (+0,04)	2,22 (+0,13)	2,15±0,12	1,71 (−0,44)	2,52 (+0,37)
TOTALS	13,5	13,6 (+0,1)	13,7 (+0,2)	18,7	23,4 (+4,7)	17,5 (+1,2)	17,4	14,4 (−3,0)	13,2 (−4,2)	18,7	10,5 (−8,2)	20,7 (+2,0)

The 175-day flight (MEC-3) also failed to elicit appreciable changes in overall free amino acid content of blood plasma, as compared to the preflight period. However, there were some fluctuations in blood amino acid levels. The CDR presented a decline in concentration of valine (1.7-fold) and methionine (2.8-fold) against a background of increase in concentration of glutamic and aspartic acids (2.8- and 2-fold, respectively); in the CDR, there was an increase in blood plasma aspartic acid (4-fold), glutamic acid (2-fold) and alanine (1.7-fold) (see Table 3).

Finally, extension of flight to 185 days (MEC-4) led to decrease in amino acid stock to levels that were below the bottom of the normal range [5]. It was more marked in the FLE. In the CDR, such a change was due primarily to decline of threonine (2-fold), serine (1.6-fold), methionine (3.4-fold) and tyrosine (2.3-fold) levels. In the CDR we found a decrease in blood plasma concentrations of 11 out of the 14 tested amino acids (see Table 3).

Analysis of the results of studying some aspects of amino acid metabolism in MEC's revealed that the decrease in stock of free amino acids of blood, against a background of individual changes in some amino acids, occurred only after missions lasting 75 and 185 days. It must be noted that in previous studies, particularly those referable to missions lasting 30 days, analogous findings were made [4]. The demonstrated decline of free amino acid levels is apparently due to specific redistribution of amino acid stock under flight conditions. Such redistribution is consistent with the conventional conceptions of the physiological role of amino acids as the body's reserve, involvement of which in numerous biochemical processes increases under the "extraordinary" conditions against a background of diminished intensity of biosynthetic processes, and this ultimately leads to a decrease in concentrations of free amino acids in blood.

It must be noted that there was a decrease in concentration levels of valine in the FLE of MEC-5, CDR of MEC-3 and FLE of MEC-4. Such changes had been also found previously among cosmonauts who had performed 30-, 48- and 63-day missions [4, 6, 7]. Apparently, this is related to nutritional factors (not eating enough, no appetite, etc.). As shown by studies with experimental protein deficiency, blood valine concentration decreases when there is less protein nitrogen in the food allowance [7]. There were less marked changes in blood aminograms of crew members who had participated in 96-, 140- and 175-day flights. This is apparently related to the fact that there was adequate inflight use of preventive measures, one of which was exercise. Indeed, in the cases where cosmonauts did not take advantage of all opportunities for exercise we observed a decrease in amino acids inherent in "extraordinary" situations (in CDR and FLE of MEC-4; CDR and FLE of MEC-5), which varied in degree. With active use of preventive exercises in flight, there was, on the contrary, an increase in concentration of aspartic and glutamic acids (in MEC-2 and MEC-3), against a background of virtually unchanged levels of free amino acids. Accumulation in blood of dicarboxylic amino acids was apparently due to developing catabolic processes. It is known that the more intensive a load, the more marked the catabolic processes, wich are the triggering mechanism for subsequent anabolic processes. We expect that the data obtained in this study of concentrations of free amino acids in blood of cosmonauts could be used in the future to assess the onboard preventive measures, in particular, the set of exercises, as well as for developing rehabilitation and

medical measures for the postflight period. Our findings revealed that the changes in amino acid composition of cosmonauts' blood plasma, which were noted in the course of the investigation, are adaptive in nature, have no pathological implications, while amino acid equilibrium is restored within 1 month after a flight.

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FREE AMINO ACIDS IN BLOOD OF SALYUT-5 CREW BEFORE AND AFTER 21-DAY MISSION (SECOND EXPEDITION)

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[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] This paper presents the measurements of free amino acids in the plasma of the Salyut-5 crewmembers (the second expedition) before and after their 21-day spaceflight. The measurements were performed in a Hitachi KLA-3B automatic amino acid analyzer. The changes in amino acid metabolism were associated with the chemical composition of the space diet, actual food intake and spaceflight effects. The conclusion is made that the dietary content of cystine and methionine, as well as phenylalanine, tyrosine, glycine, glutamic acid and serine should be increased. No signs of hepatic or renal dysfunction were detected. It is recommended to control strictly food consumption inflight.

[Text] Free amino acid levels in human and animal blood plasma are subject to changes under the influence of various endogenous and exogenous factors: intensity and direction of metabolism, condition of the liver, kidneys and other organs, amount and composition of food, etc. Apparently, the range of such changes could be quite significant, depending on the condition of the body and nutritional status at a given time, prior diet and food allowance, nature of ambient factors to which man is exposed, as well as individual constitutional distinctions. This is indicated, for example, by the quite significant fluctuations in concentrations of plasma free amino acids, which are cited by many authors as guidelines for healthy adults [1-4]. At the same time, there has been insufficient investigation of the degree of effects of different environmental factors, particularly, diet, working conditions, individual state of metabolism on concentration of free amino acids in human blood plasma. In particular, amino acid metabolism as affected by the set of factors involved in orbital flight is one of the least studied aspects of cosmonaut metabolism [5-7].

We submit here the results of an investigation of free amino acid levels in blood plasma of the commander (CDR) and flight engineer (FLE) of the Salyut-5 orbital station (second expedition) before and after their 21-day flight.

Methods

We assayed free amino acids in blood plasma of the crew of Salyut-5 station (second expedition) taking samples of venous blood on a fasting stomach, before the flight, during a scheduled clinical and physiological work-up and then on the 1st day after termination of their 21-day mission. Standard methods were used to prepare blood and plasma samples [7-10]. Amino acids were assayed with a Hitachi (KLA-3B model) automatic amino acid analyzer. In the opinion of prominent contemporary clinicians and biochemists, a precise answer can be obtained about amino acid levels in blood with use of such an automatic analyzer [2, 10]. We considered the dynamics of amino acid concentrations and compared them to data of other authors.

Results and Discussion

Table 1 lists concentrations of free amino acids in blood plasma of the CDR and FLE of the Salyut-5 station (second expedition) before and after their 21-day orbital flight. The data it contains lead to the conclusion that the absolute majority of essential and nonessential amino acids were present in blood plasma of both cosmonauts before the flight in concentrations within the range of "Approximate Data for the Adult Population" [1]. The only exceptions were cystine and aspartic acid, whose levels in plasma were lower in the cosmonauts. Plasma cystine level was 0.29 mg% lower in the CDR and 0.26 mg% lower in the FLE than the bottom of the range indicated in BME [Great Medical Encyclopedia] [1]. This could have been attributable to the distinctions of the preflight diet of the cosmonauts. In the crew of the first expedition aboard Salyut-5, plasma cystine level was also below normal during the preflight training period and with an analogous food allowance [1]. B. I. Zbarskiy et al. [2, 3] cite even higher figures as the physiological norm for plasma cystine content (in the range of 2.0-3.0 mg%). As compared to the data of those authors, the concentration of cystine in plasma of the crew of Salyut-5 was even lower than in comparison to the figures of I. S. Balakhovskiy. It should be noted that some authors, who used ion-exchange chromatography to test individuals in other occupational groups, also found lower concentrations of cystine in plasma than those cited in [1-3]. For example, R. A. Zhagat and R. F. Platniyetse [11], who tested 10 adults, found that their plasma cystine level constituted a mean of 0.8 mg%, with standard deviation of ±0.18. The concentration of cystine that they demonstrated was close to the levels we found in cosmonauts. At the same time, Muller [4], who also assayed amino acids by the ion-exchange method on columns, cites higher figures for blood plasma cystine, although they were referable to individuals tested under other conditions: from 1.15 to 3.37 mg% (average 1.77 mg%). A. S. Ushakov and T. V. Vlasova [5] found levels in cosmonauts that were close to ours, 0.73±0.04. All this confirms the role of the chemical composition of diet and influence of occupational and other living factors on metabolism as a whole, concentration of cystine and, probably, other amino acids in plasma. In the comparative physiological and hygienic aspect, the cystine concentration in plasma of the CDR and FLE in the preflight period should be deemed as being somewhat low or close to the bottom of the normal range proposed by several authors [1-4]. The fact that the cystine concentration was quite similar in both crew members (0.71 and 0.74 mg%), and that it was close to figures demonstrated in other cosmonauts [6] is indicative of the

identical cause of this phenomenon. The similar chemical composition of the diet and similar physical loads could be such a cause.

Table 1. Free amino acid levels (mg%) in blood plasma of crew of Salyut-5--Soyuz-24 space complex (second expedition) before and after 21-day mission

AMINO ACIDS	"APPROX. BLOOD PLASMA AMINO ACID LEVELS IN ADULTS" INDICATED IN BME [1]	AMINO ACID CONTENT OF BLOOD PLASMA OF COSMONAUTS					
		CDR			FLE		
		PRE-FLIGHT	FIRST POST-FLIGHT DAY	CHANGE IN FLIGHT	PRE-FLIGHT	FIRST POST-FLIGHT DAY	CHANGE IN FLIGHT
A. ESSENTIAL AMINO ACIDS:							
LYSINE	1,0—4,0	3,42	3,68	+0,26	3,03	3,22	+0,19
THREONINE	1,0—3,0	1,60	1,62	+0,02	1,98	1,78	—0,20
VALINE	1,5—3,0	2,22	2,41	+0,19	2,71	2,59	—0,12
METHIONINE	0,3—0,7	0,39	0,35	—0,04	0,47	0,37	—0,10
LEUCINE	1,0—3,0	1,79	1,85	+0,06	1,33	1,45	+0,12
ISOLEUCINE	0,5—1,0	0,80	0,99	+0,19	1,09	1,00	—0,09
PHENYLALANINE	0,5—2,0	1,09	0,86	—0,23	1,04	0,89	—0,15
B. NONESSENTIAL AMINO ACIDS:							
CYSTINE	1,0—3,0	0,71	0,45	—0,26	0,74	0,59	—0,15
TYROSINE	0,6—2,0	1,05	1,00	—0,05	1,09	0,87	—0,22
ALANINE	2,0—4,0	2,75	2,92	+0,17	3,11	2,99	—0,12
ARGININE	1,0—3,0	0,92	1,31	+0,39	1,17	1,88	+0,71
ASPARTIC ACID	2,0—5,0	0,14	0,18	+0,04	0,21	0,13	—0,08
HISTIDINE	0,8—2,0	1,68	1,57	—0,11	1,31	1,31	0
GLYCINE	1,0—4,0	1,96	1,12	—0,84	1,81	1,42	—0,39
GLUTAMIC ACID	0,7—4,0	2,71	2,08	—0,63	2,69	2,48	—0,21
PROLINE	0,5—3,0	1,69	1,92	+0,23	1,98	1,47	—0,51
SERINE	1,0—2,0	1,33	1,27	—0,06	1,51	1,44	—0,07

The concentration in plasma of methionine, metabolism of which is closely linked to metabolism of cystine [3], was within the range given in BME [1] before the flight. This is not indicative of a significant cystine deficiency in the diet or body. However, methionine content in the organism was sooner on the average level, rather than the highest one, particularly in the CDR. Interestingly, some others also observed a low cystine content, which differed little from our figures (0.8±0.18 mg% cystine), with similar methionine content of plasma (0.38±0.07 mg%) [11]. At the same time, other researchers, who demonstrated a similar amount to ours of plasma methionine (0.32 mg%; from 0.23 to 0.39 mg%), demonstrated higher concentrations of cystine (1.77 mg%; from 1.15 to 3.37 mg%) [4]. This confirms the fact that low cystine content leads to decrease in plasma methionine concentration; however, a high cystine level in the body does not guarantee against development of methionine deficiency. A. S. Ushakov and T. F. Vlasova [5], who found the same cystine content in other cosmonauts as we did, demonstrated a lower methionine level, 0.26±0.01 mg%.

Aspartic acid content of blood plasma was much lower in both cosmonauts than cited in BME [1]: aspartic acid concentration was 0.14 mg% for the CDR and 0.21 mg% for the FLE. In analyzing the obtained data (see Table 1), it should be noted that other researchers, who also used ion-exchange chromatography on an automatic analyzer, found aspartic acid levels in plasma that were closer to our findings, namely, 0.16±0.02 mg% [11], 0.11±0.01 mg% and even 0.07±0.05 mg% [5, 6] than to the above-mentioned "approximate standards" [1]. Other researchers, who used a Czech automatic analyzer, demonstrated low levels of aspartic acid in blood plasma, but somewhat higher than in our cosmonauts--0.39 mg% [12]. Relatively higher concentrations of aspartic acid, but still lower than cited in BME [1], are also encountered in other studies where paper chromatography was used [13]. Evidently, the method of investigation is very important. For this reason, the demonstrated concentrations of aspartic acid in the cosmonauts cannot be taken as evidence of a deficiency in this amino acid. The demonstrated level of aspartic acid is probably attributable to living conditions and diet of the examined cosmonauts, since its plasma concentrations were similar in the CDR and FLE, and were close to the preflight levels found in plasma of Salyut-5 crew members (first expedition; 0.11 and 0.32 mg%) [7] and the data cited by A. S. Ushakov and T. F. Vlasova.

It should be noted that the plasma levels of all amino acids before the flight did not exceed figures cited by most authors [1-4], which confirms the good functional state of the liver and kidneys of both cosmonauts.

The concentration of absolute majority of amino acids remained in the normal range for both cosmonauts immediately after completion of the 21-day flight [1]. According to the data in Table 1, the only exceptions were the same cystine and aspartic acid, the concentration of which was below the bottom of the range indicated in the "approximate data" [1] after the flight. We cannot fail to mention that cystine concentration was even lower postflight in both cosmonauts than preflight: by 0.26 mg% for the CDR and 0.15 mg% for the FLE. As compared to the "approximate data" [1], plasma cystine content postflight was below the bottom of their range, by 0.55 mg% for the CDR and 0.41 mg% for the FLE. After the flight, the CDR also presented a somewhat lower cystine level in plasma than the FLE. The strained cystine metabolism in both cosmonauts and, perhaps, some deficiency thereof, also confirm the decrease they demonstrated postflight in plasma methionine concentration. It was less significant in the CDR and more noticeable in the FLE. One of the probable causes of this phenomenon is the decreased intake of cystine and methionine with the foods contained in the flight diet. As we know, the onboard food allowances of cosmonauts contained canned meat and dairy products, the amino acid composition of which is considered limited in cystine and methionine. It should be mentioned that A. S. Ushakov and T. F. Vlasova, who used an analogous method [6], previously demonstrated a decrease in plasma cystine and methionine levels in cosmonauts following their 30-day mission aboard Soyuz-17.

There was postflight increase by 0.04 mg% in aspartic acid content of plasma in the CDR, whereas in the FLE it decreased by 0.08 mg%, which could be indicative of insignificant influence of flight conditions on resources referable to this amino acid in cosmonauts. After the flight, the aspartic acid concentration was, as before, substantilly lower than listed in the "approximate data" in BME [1]. This requires further clarification, in particular, of

the question of how "physiological" is the bottom of the range in the above-mentioned "approximate data."

We also demonstrated a decrease, in comparison to preflight values, in concentrations of the following amino acids in plasma of both cosmonauts taken immediately after the flight: phenylalanine (by 0.23 and 0.15 mg% in the CDR and FLE, respectively), tyrosine (by 0.05 and 0.22 mg%), glycine (by 0.84 and 0.39 mg%), glutamic acid (by 0.63 and 0.21 mg%) and serine (by 0.06 and 0.11 mg%). Histidine concentration decreased (by 0.11 mg%) only in the CDR. This parameter remained unchanged in the FLE. Conversely, threonine concentration diminished by 0.20 mg%), as did valine (by 0.12 mg%), isoleucine (by 0.09 mg%), alanine (by 0.12 mg%) and proline (by 0.51 mg%) only in the FLE. There was an increase in concentrations of the following amino acids in the CDR: threonine (by 0.02 mg%), valine (by 0.19 mg%), isoleucine (by 0.19 mg%), alanine (by 0.17 mg%), proline (by 0.23 mg%), lysine (by 0.26 mg%), leucine (by 0.06 mg%) and arginine (by 0.39 mg%). In the FLE there was increase in plasma lysine (by 0.19 mg%), leucine (by 0.12 mg%) and arginine (by 0.71%).

Thus, we demonstrated changes in different directions for the five amino acids (threonine, valine, isoleucine, alanine and proline), but they were minor and did not exceed the range mentioned in the "approximate data" in BME [1], and apparently they are attributable to physiological fluctuations of amino acid metabolism. The relatively good supply of these amino acids in the cosmonauts during the preflight period and the flight itself was apparently instrumental in this. In both crew members, we demonstrated an increase in concentrations of plasma lysine (by 0.26 mg% for the CDR and by 0.19 mg% for the FLE), leucine (by 0.06 and 0.12 mg%) and arginine (by 0.39 and 0.71 mg%) after the flight. It should be mentioned that during this flight there was no decline of arginine, as had been reported by other authors [6].

The amount of amino acids in blood plasma increases when there are diseases and functional changes in the liver, which is related to diminished urea synthesis. This is associated with a particular increase in concentrations of cystine, cysteine, methionine, tyrosine and glutamic acid [2]. According to the data in Table 1, the concentrations of these amino acids, on the contrary, either diminished or underwent virtually no change during the flight. There was some increase in concentrations of another group of amino acids--lysine, leucine and arginine.

The overall (general) indicators of levels of 17 amino acids in blood plasma of the crew aboard the Salyut-5 orbital research station before and after their 21-day mission are listed in Table 2. The same table lists overall parameters, which we calculated on the basis of the "approximate data on amino acid levels in blood plasma of adults," cited in BME [1].

According to the data in Table 2, it can be concluded that the sum of essential amino acids was rather similar in both cosmonauts, and it was greater by only 0.34 mg% in the plasma of the FLE. It corresponded approximately to the average (11.4 mg%) sum of essential amino acids calculated on the basis of data in [1]. After the flight, this parameter increased by 0.45 mg% for the CDR and decreased by 0.35 mg% for the FLE. Such change in total essential amino acids is attributable to the rise in levels of 5 out of 7 amino acids in the CDR and, on the contrary, to decrease in concentration of 5 out of 7 amino acids in the FLE.

After the flight, the sum of essential amino acids remained close to the average (11.4 mg%) calculated from the data in [1]. The difference between the CDR and FLE in this parameter constituted 0.34 mg% before the flight and 0.46 mg% after.

Table 2. Overall (general) parameters of 17 free amino acid levels in blood plasma of crew members aboard the Salyut-5 orbital research station (second expedition) before and after 21-day flight (mg%)

PARAMETERS OF AMINO ACID METABOLISM	CDR			FLE			GENERAL PARAMETERS CALCULATED ON BASIS OF "APPROXIMATE DATA" IN BME [1]
	PRE-FLIGHT	POST-FLIGHT	CHANGE IN FLIGHT	PRE-FLIGHT	POST-FLIGHT	CHANGE IN FLIGHT	
TOTAL ESSENTIAL AMINO ACIDS (E)	11,31	11,76	+0,45	11,65	11,30	—0,35	16,4—48,7
TOTAL NONESSENTIAL AMINO ACIDS (N)	14,94	13,82	—1,12	15,62	14,58	—1,04	10,6—32,0
TOTAL AMINO ACIDS (E+N)	26,25	25,58	—0,57	27,27	25,88	—1,39	16,4—48,7
ESSENTIAL TO NONESSENTIAL AMINO ACIDS RATIO (E/N)	0,75	0,85	+0,10	0,74	0,77	+0,03	0,55—0,52

The sum of nonessential amino acids was also quite similar in the cosmonauts before the flight (0.68 mg% more in FLE plasma). It corresponded approximately to the average (16.53 mg%) calculated on the basis of the "approximate data" in BME [1], particularly for the FLE. We should call attention to the fact that the sum of nonessential amino acids presents a wider scatter of values, according to some authors [1, 10, 11] than the sum of essential amino acids. It is not surprising that the sum of nonessential amino acids differed more in the CDR and FLE than the sum of essential amino acids. After the flight, this parameter decreased by 0.04 mg% for the CDR but, as before, was higher in the FLE--by 0.76 mg%, i.e., by virtually the same amount as in the preflight period. Consequently, the change in sum of nonessential amino acids occurred in the same direction. It occurred due to decrease, in both cosmonauts, in cystine, tyrosine, glycine, glutamic acid and serine content. The decrease in histidine content in the CDR, and in alanine, aspartic acid and proline content in the FLE was also of some significance. As compared to the average sum of nonessential amino acids [1], this parameter decreased somewhat after the flight. This decline could be due to both insufficient intake with food and increased outlay thereof by the body, and this requires attention, as well as special physiological and hygienic evaluation.

In both cosmonauts, the overall sum of plasma amino acids was somewhat lower than the average calculated from the "approximate data" in BME [1] before the flight, which was 32.55 mg%. In the CDR this parameter was 6.3 mg% lower and in the FLE 5.28 mg% lower. After the flight, total amino acids decreased by 0.57 mg% for the CDR and 1.39 mg% for the FLE. Consequently, total amino acids of plasma diminished in both cosmonauts after the flight. This decline was more significant in the FLE due to the fact that he presented a decrease in concentrations of both essential and nonessential amino acids. In the CDR, we demonstrated a decrease in nonessential amino acids, by an amount similar to the one found for the FLE, but against a background of increase in essential amino acids.

The ratio of essential to nonessential amino acids (E/N) was higher before and after flight in both cosmonauts than for concentrations of amino acids on the level of the bottom and top range of "approximate data" in BME [1] or average E/N of 0.53. This is attributable, for the CDR, to the decrease in plasma nonessential amino acids, with increase in essential ones.

In the preflight period, this ratio can be explained by the relatively lower levels of nonessential amino acids, as compared to essential.

The postflight increase in E/N in the CDR was due to a decrease in nonessential amino acids with increase in essential ones, whereas in the FLE there was more intensive decrease in nonessential amino acids than essential ones. While the preflight E/N ratio was virtually the same for the CDR and FLE, after the flight it was higher in the CDR due to decrease in nonessential and increase in essential amino acids. On the whole, the E/N parameter was better in the CDR.

On the basis of our analysis of data obtained from testing the crew of Salyut-5 (second expedition) before and after their flight, the following conclusions can be drawn.

Overall sum of amino acids in blood plasma diminished in both cosmonauts after the 21-day mission. This decline was more marked in the FLE, due to decrease in sum of essential and nonessential amino acids. In the CDR, there was even increase in sum of essential amino acids. Such dynamics of these overall parameters could be attributed both to decreased intake of amino acids with the flight food allowance and increased requirements of the body. This applies, first of all, to nonessential amino acids, the sum of which in plasma decreased in both cosmonauts. As for essential amino acids, the different directions of their changes apparently reflect individual metabolic distinctions of the cosmonauts, as well as qualitative and quantitative characteristics of their actual food intake during the flight. There is reason to believe that the FLE consumed less food during the flight than the CDR. This is confirmed by the fact that the CDR lost 3.5 kg during the flight and the FLE lost 3.9 kg. On the first postflight day, elimination of total nitrogen in urine constituted 20.4 g for the CDR and 11.9 g for the FLE; potassium excretion constituted 82.5 and 51.6 meq, respectively. These data are an indication, to some extent, of the fact that the CDR consumed somewhat more protein-containing foods (meat and dairy products). Hence, improvement and increase in amino acid composition of the food allowance for the FLE could play some preventive role.

On the other hand, it is imperative to keep a strict regard of actual inflight food intake for correct and objective interpretation of results of biochemical studies of metabolic parameters in cosmonauts beofre and after flight, for the purpose of physiological and hygienic evaluation of the effects of flight factors on dynamics of metabolism.

The study of concentration of different amino acids in plasma and their dynamics under the influence of the factors involved in the flight in question compels us to call attention primarily to cystine and methionine content. In this respect, our data conform to the results of A. S. Ushakov and T. F. Vlasova, which were obtained with reference to other flights [5, 6]. Evidently,

the amounts of these amino acids should be increased in both the preflight and inflight food allowances for cosmonauts. Moreover, a positive effect could be obtained by increasing also the amounts of phenylalanine, tyrosine, glycine, glutamic acid and serine in the onboard food allowance, since their concentrations diminished in both cosmonauts after the flight.

The dynamics of amino acid levels in blood plasma are also indicative of the fact that no gross changes occurred in liver and renal functions during the flight, which could have had a serious influence on increasing amino acid concentrations in blood or led to decreased excretion of amino acid nitrogen.

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NUTRITIONAL STATUS WITH USE OF CHOCOLATE AS EMERGENCY RATION

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[Article by I. G. Popov, P. A. Lozinskiy, A. A. Latskevich and I. A. Romanova]

[English abstract from source] Using the results of studying the body mass, carbohydrate, amino acid, nitrogen and mineral metabolism, as well as the general health status of test subjects who were on a low-caloric diet of 300 g chocolate, it is concluded that, although their condition and nutritional status remained satisfactory, chocolate in the above quantity can hardly be viewed as an ideal emergency food for pilots. The conclusion is based on the metabolic and operational limitations of chocolate. The study was carried out in a temperate climate with water consumption of no more than 1 ℓ per day.

[Text] Chocolate has long since been used extensively in emergency packs serving the most varied purposes, including onboard emergency supplies (OES) and portable emergency supplies (PES) carried by aircraft and spacecraft crews. As far back as 1936, one of the first Soviet "food supplies for forced landings far from populated areas," included chocolate (300 g), along with biscuits (300 g) and canned meat (340 g). This emergency kit for 1 person consisted of 3052 kcal. According to one of its developers (S. S. Kholin), this pack was intended for use in emergency situations for 3 days [1, 2].

During the Great Patriotic War (starting in 1941), emergency food supplies were used on all types of aircraft, and they included 300 g chocolate [3], in addition to other foods (biscuits, condensed milk, canned meat, sugar).

In foreign aircraft PES, chocolate was also generally included as one of the "survival" foods in unpopulated regions [4, 5]. At the present time, as before, chocolate is used extensively in emergency supplies for pilots, cosmonauts, seamen, etc. In particular, there is the so-called PES-u, in which 300 g chocolate is the only food, not counting table salt (60 g) packaged in a separate polyethylene bag [6]. Such a PES is intended for use for 3-5 days.

Chocolate has attracted the attention of developers of emergency supplies primarily because of its high caloric value. Indeed, the energy value of

different brands of chocolate is relatively high, ranging from 540 to 557 kcal/100 g (2259-2330 kJ), whereas in powdered chocolate it is 483 kcal (2021 kJ) [1]. This is due to the fact that chocolate also contains fat, in addition to carbohydrates and protein. Also, chocolate contains macroelements, including potassium and phosphorus, small amounts of vitamins B_1, B_2 and PP. It is also of definite relevance that chocolate has a good flavor.

However, chocolate also has some serious operational flaws. They include, first of all, its limited shelf life and rapid loss of "marketable appearance." Moreover, chocolate softens at high ambient temperature due to its low melting point. One gets thirsty after eating chocolate, and this is undesirable when water supply is limited. In a number of cases, there may be difficulties with regard to manufacture and supply.

We were impressed, after analyzing the reasons for including chocolate in emergency rations, as well as its use in aviation and cosmonautics, by the fact that there is prevalence of theoretical considerations in the recommendations for its use. There are virtually no experimental data in the literature dealing with evaluation of the dynamics of the nutritional status of man when consuming "survival" rations consisting of chocolate alone [5].

We submit here the results of a physiological and hygienic assessment of dynamics of nutritional status of subejcts who spent 5 days on a low-calorie "survival" diet, consisting only of 300 g chocolate.

Methods

We studied the dynamics of nutritional status of subjects under simulated conditions of an "emergency situation."

On the day of take-off, the subjects were given the standard preflight breakfast containing a total of about 1017 kcal, with 43 g protein, 46 g fat, 115 g carbohydrates and 400 mℓ fluid (200 mℓ in the form of tea and 200 mℓ as juice). The breakfast weighed a total of 505 g. In accordance with the established preflight schedule, 1.5 h after breakfast we recorded the start of the "flight," and 2 h later we declared an "emergency landing," after which only the emergency supplies were used for 5 days as the source of food and fluid.

The emergency rations for each subject for the 5-day period consisted of only 300 g chocolate, as provided in one of the versions of aircraft PES, the so-called PES-u [6]. We used the Sport brand of chocolate (GOST 65 34-69), which is often used in aircraft PES. The nutritional value of 300 g of Sport chocolate is 1671 kcal (6990 kJ), and it contians 22.8 g protein, 111.6 g fat, 152.4 g carbohdyrates, 231 mg Na, 1335 mg K, 0.87 mg B_2, 645 mg Ca, 105 mg Mg, 678 mg P, 3.9 mg iron, 0.18 mg B_1 and 1.14 mg PP [7].

During the "survival" period, all of the subjects consumed the emergency supply of chocolate in accordance with a previously established mealtime schedule. On the evening of the first day of the "emergency landing," they received 20 g chocolate at 1900 hours. Thus, there was a 10-h interval between the preflight breakfast and food intake with the first emergency "supper." For

the next 4 days, they were issued 70 g chocolate per day. The daily portion of chocolate was divided into three meals: 20 g at 0900, 30 g at 1400 and 20 g at 1900 hours. The subjects received water at the rate of 1 ℓ per day. With the exception of the first day, we "ran" through the emergency ration situation on all subsequent days, during which intake of food concided with the customary times for the subjects of having breakfast lunch and supper, in order to preserve the previously formed stereotype of digestion.

We counted the beginning of each successive day during the experiment at 0800 hours, after collecting noctural urine for the preceding day. The distinction of the first day was that it started at 0800 hours, before the preflight breakfast and ended at 0800 hours the following morning, already in the "emergency survival" period, after consuming the "emergency supper." The 5th day of the studies ended at 0800 hours on the morning of the 6th day, counting from the beginning of the studies. Thus, the subjects were on a mixed diet on the first day, including preflight and "emergency" food. For the next 4 days they received only the emergency food. This procedure conformed to conditions that could develop in a real emergency situation.

A total of 7 men participated in our studies, 35-40 years of age, which had undergone a physical and were deemed essentially healthy. They had all been informed about the hygienic distinctions of low-calorie food allowances, in order to provide psychological and special preparation for "emergency survival."

We examined the nutritional status of the subjects according to the following parameters: body weight, carbohydrate, nitrogen, amino acid and mineral metabolism, fluid intake, diuresis. We recorded data concerning their well-being by means of a questionnaire, as well as data obtained from medical supervision of their general physical condition. Special attention was devoted to their appetite, sensation of thirst, acceptability of the food and whether they became tired of it.

During the test period, the subjects continued to perform their customary work, which did not involve any considerable physical exertion, constituting energy expenditure of 3000-3200 kcal/day, i.e., within the range of daily energy expenditure for the first occupational group, according to the physiological nutrition standards of the USSR Academy of Medical Sciences in 1968 [8]. Living conditions were typical for a large modern city with well-developed municipal services. These studies were conducted in the spring, in the temperate climate zone of European USSR.

Results and Discussion

Table 1 lists the results of determining weight dynamics of the subjects when kept for 5 days on emergency rations consisting only of 300 g chocolate. The data in this table or summarized for two "survival" terms under emergency conditions: 3 and 5 days. According to these data, the subjects continuously lost weight during the 5 days. This was due primarily to the quantitative shortage of food. The subjects presented energy expenditure of 3000-3200 kcal/day per 70 kg weight, whereas their rations amounted to 1128.4 kcal on the first day (counting the preflight breakfast, 1017 kcal, and 111.4 kcal from 20 g chocolate), 389.9 kcal on the 2d to 5th days, from 70 g chocolate per day.

Table 1. Dynamics of subjects' body weight on low-calorie chocolate rations (n = 7)

No	Subjects	Height, cm	Initial weight, kg	Body wt according to Broca index	Weight loss, kg (percentage of initial wt shown in parenth.) — Day on low-calorie diet							Weight after 5 days, kg	Recommended wt of A. Pokrovskiy [19], kg
					1	2	3	1—3	4	5	1—5		
1	P-YEV	178	84,50	+6,50	1,95 (2,31)	1,40 (3,97)	0,70 (4,80)	4,05 (4,80)	0,30 (5,16)	0,35 (5,56)	4,70 (5,56)	79,80	79,80
2	L-IY	184	84,45	+0,45	1,45 (1,72)	0,95 (2,85)	0,85 (3,86)	3,25 (3,86)	0,65 (4,63)	0,40 (5,09)	4,30 (5,09)	80,15	79,20
3	T-KO	183	80,50	−2,50	1,40 (1,74)	1,00 (2,98)	1,00 (4,22)	3,40 (4,22)	0,60 (4,97)	0,55 (5,65)	4,55 (5,65)	79,95	77,20
4	KH-OV	172	79,35	+7,35	1,30 (1,67)	1,40 (3,43)	0,35 (3,87)	3,05 (3,87)	0,55 (4,52)	0,75 (5,48)	4,35 (5,48)	75,00	69,70
5	L-ICH	172	75,50	+3,50	1,40 (1,85)	0,80 (2,91)	0,65 (3,77)	2,85 (3,77)	0,60 (4,72)	0,60 (5,53)	4,10 (5,09)	71,40	69,70
6	V-YETS	178	74,10	−3,90	1,15 (1,55)	0,95 (3,98)	0,95 (4,11)	3,05 (4,11)	0,45 (4,72)	0,60 (5,53)	4,10 (5,53)	70,00	67,30
7	N-OV	169	72,45	+3,45	1,66 (2,28)	1,20 (3,94)	0,45 (4,56)	3,30 (4,56)	0,50 (5,25)	0,35 (5,73)	4,15 (5,73)	68,30	67,80
	M±m				1,47±0,11 (1,95±0,09)	1,10±0,08 (3,44±0,10)	0,71±0,09 (4,17±0,14)	3,28±0,17 (4,17±0,14)	0,52±0,05 (4,83±0,10)	0,49±0,06 (5,46±0,09)	4,29±0,11 (5,46±0,09)		

Table 2. Dynamics of blood glucose content during 5-day low-calorie chocolate rations (n = 7)

No	Subjects	Broca index for body weight	Blood glucose content, mg% — Day on low calorie diet (when blood was taken)											Third day after test	
			1		2		3		4		5		6		
			Blood taken at (time of day)												
			9.00*	18.00	9.00	18.00	9.00	18.00	9.00	18.00	9.00	18.00	9.00**	9.00	18.00
1	P-YEV	+6,50	86	69	70	54	64	53	54	55	57	68	68	78	89
2	L-IY	+0,45	88	99	66	78	74	58	68	52	53	49	59	63	65
3	T-KO	−2,50	96	79	56	79	74	52	67	48	51	74	57	63	61
4	KH-OV	+7,35	92	66	58	69	59	98	51	58	62	65	55	88	72
5	L-ICH	+3,50	66	93	53	68	91	53	78	52	58	55	65	63	71
6	V-YETS	−3,90	88	106	63	96	71	53	83	52	60	49	73	65	68
7	N-OV	+3,45	68	68	55	52	70	51	49	55	51	62	59	74	77
	M±m		83,4±4,85	82,9±6,46	60,1±2,75	70,9±7,11	71,9±5,17	60,0±7,43	64,3±5,49	53,1±1,62	56,6±1,78	56,0±3,88	62,3±2,91	70,6±4,04	73,3±4,52

*Fasting, before preflight breakfast.
**Fasting, end of 5th day of study.

It was inevitable for endogenous supplies of nutrients--carbohydrates, protein and fat--to be used to compensate for the energy (caloric) deficiency. Loss of fluid also had a definite effect on weight loss. Since the temperature was close to the comfortable level, the main loss of fluid should have been referable to diuresis, and this was observed in the studies. Fluid loss referable to urine usually demonstrates a particular increase on the first day of starvation when changing to a low-calorie diet. In our case, the most intensive loss of fluid referable to diuresis was also observed on the 1st and, in part, the 2d day on the low-calorie diet. Accordingly, there was maximum weight loss on the 1st (1.95 to 1.15 kg, average 1.47±0.11 kg/day) and 2d days (1.4 to 0.9 kg, average 1.10±0.08 kg/day). Thereafter, there was gradual decrease in daily weight loss, and for the entire group it averaged 0.7±0.09 kg on the 3d day, 0.52±0.05 kg on the 4th and 0.49±0.06 kg on the 5th day. These data also indicate that individual differences in weight loss leveled off as the subjects continued the low-calorie diet. The decrease in body weight during the first 2 days was also greatest, when determined as a percentage. While the weight loss for the first 3 days constituted an average of 4.17±0.14% for the group, it was 3.44±0.10% for the first 2 days. In 5 days, this parameter reached 5.46±0.09%. The weight loss observed for 5 days should be assessed as moderate, far from the critical level of 40% loss of initial weight, which is hazardous to health and life. If we compare body weight to the data on its dynamics during starvation, we can conclude that all of the subjects were at the early stage of quantitatively malnutrition and adaptation to low-calorie diet.

As would be the case in a real situation, the initial nutritional status of the subjects was not the same for all. It can be concluded from the data in Table 1 that, according to the Broca index, four of the subjects were overweight at the initial period, one had a normal weight and two were underweight. After the 5 days on a low-calorie diet, the two subjects who weighed the most still presented above normal body weight, two retained a weight in the normal range (-0.6 and -0.7) and three had a weight that was below normal (according to Broca's index). Judging by this parameter, the subjects who weighed less in the initial period were in the poorest situation after 5 days on a low-calorie diet (subjects Nos 6, 3 and 2 in Table 1).If we compare the data to the recommended normal weight levels for adult males, according to A. A. Pokrovskiy [9], all of the subjects had an initial weight above the recommended level. Weight was still above normal in 6 subjects after 5 days on a low-calorie diet, and it remained on the recommended level in only 1 case.

Thus, the submitted data confirm the above conclusion, to the effect that, on the tested type of emergency rations, all of the subjects did not have such significant weight loss or such a quantitative change in nutritional status after 5 days as to cause the quantitative shortage of food to have an excessive effect on their health and work capacity in this time. It should be noted that, judging by the quantitative index of Broca, subjects whose initial weight was below normal were in the worst situation.

Table 2 lists the results of assaying blood sugar in the subjects who were on emergency rations. Blood was taken from the finger twice a day, daily, before breakfast and supper. Blood glucose was assayed by the glucose oxidase method as modified by I. S. Balakhovskiy, in which samples of capillary blood are taken, put on filter paper and then desiccated. With this method, a glucose concentration of 70±10.7 mg% is taken as normal, which is rather close

to the normal levels with the ordinary clinical modification of the glucose oxidase test (56-94 mg%) [10]. According to Table 2, on the first day of the "emergency situation," after changing to the low-calorie chocolate diet, blood glucose level was not below the physiological norm, and was even above it in some subjects. On the morning of the 2d day, glucose concentration was appreciably lower in all subjects than the preceding morning before the preflight breakfast, and in 4 out of 7 subjects it was below normal. Hypoglycemia was found on the evening of the 2d day in only 2 subjects. On the 3d day, glucose concentration was below normal in the morning in 1 subject and in the evening in 6 out of 7; on the 4th day, it was below normal in the morning in 3 cases and in all 7 subjects in the evening; on the 5th day it was low in the morning in 5 people and in the evening in 3. Fasting blood sugar was below normal at 0900 hours on the 5th day in 4 subjects, prior to the end of the emergency diet. On the 3d day after terminating the studies, no cases of hypoglycemia were demonstrable. However, blood sugar was lower in most subjects than the fasting level in the morning before the preflight breakfast before we started this test. The mean figures for the group of subjects are also indicative of gradual decline of blood sugar with increase in duration of low-calorie diet. Starting on the evening of the 4th day, mean figures were on the hypoglycemic level. It is only on the morning of the 6th day, before terminating the low-calorie diet, that the mean blood sugar concentration returned to the normal range. This phenomenon could be related to some stress due to termination of the unusual and uncomfortable studies.

Thus, intake of 300 g chocolate in 5 days did not eliminate the possibility of development of sporadic hypoglycemia (starting on the 2d day), appearance of which was increasingly frequent as the low-calorie diet continued.

The stock of carbohydrates in the human body is small, so that amino acids and endogenous body fats are utilized for energy purposes when on a low-calorie diet or complete fast. With fasting, low-calorie or carbohydrate-free diet, there is depressed utilization of acetyl CoA in the tricarboxylic acid cycle and fatty acid synthesis, since all of the body's metabolic resources are converted into blood glucose. As a result, there is increased synthesis of ketone bodies. Intake with food of ketogenic amino acids, certain proteins and fats is instrumental in intensive synthesis of ketone bodies [11-13]. Accumulation of ketone bodies, along with acidosis that is caused by this process, as well as hypoglycemia, are considered among the prime causes of poorer well-being (general weakness, headache, vertigo, etc.) and diminished work capacity when on a low-calorie diet, particularly at early stages [14, 15]. Ketonemia is usually associated with ketonuria; for this reason, one can assess from the latter the intensity of formation of ketone bodies in the body and amount thereof in blood. When on a low-calorie diet, the intensity of ketonuria enables us to assess the extent of oxidation of endogenous fat supply and fats and amino acids contained in taken food [11, 15, 16].

Examination of excretion of ketone bodies in urine using our modification of the method of Ember and Bonnamur [17] revealed that no ketone bodies were demonstrable in urine in the base period and on the first day of emergency rations. In urine collected on the 2d day of emergency rations, ketone bodies were found in 4 out of 7 subjects. On the 3d-5th days, ketone bodies were

present in urine of all subjects, presenting a tendency toward increase. Thus, while ketone bodies were excreted in urine in amounts of 166-300 mg/day on the 2d day, the figures ranged from 868-1261 mg/day for the 3d-5th days. Consequently, when using the "chocolate" emergency rations, starting on the 2d day, the endogenous supply of carbohydrates, as well as intake of carbohydrates with the chocolate, were no longer sufficient to avert ketonemia. The fat in chocolate, as well as protein, could intensify production of ketone bodies when there is a general carbohydrate deficiency [11].

Our data are consistent, to some extent, with the results of M. N. Logatkin and H. Drury , obtained using other types of low-calorie diets [14, 18]. The signs of hypoglycemia, which were observed in our subjects starting on the 2d day on the emergency diet, were generally consistent with development of ketonuria at the same period.

Free amino acid levels in blood plasma of fasting subjects on the 1st day, before the preflight breakfast and at the same time of day (0800 hours) at the end of the 5th day on the emergency rations were assayed by ion-exchange chromatography, using the Hitachi KIA-3B automatic analyzer. The results are listed in Table 3. The levels of most amino acids before going on the emergency diet were in the range of the usual average values cited by I. S. Balakhovskiy in the third edition of BME [Great Medical Encyclopedia] [19]. The only exceptions were lysine, whose concentration in plasma was above "normal" in some subjects, and cystine, the concentration of which was below the approximate "norm" listed in BME [19] in all of the subjects. We made a comprehensive study of the causes of decrease in cystine and aspartic acid content of plasma in a work dealing with amino acid levels in blood of cosmonauts [20]. In this case, the causes are apparently the same: decline of cystine was attributable to the distinctions of the preflight diet. With regard to aspartic acid, it is necessary to clarify the bottom range of the "physiological norm" given in BME [19]. The relatively low concentration of methionine confirms, to some extent, the low supply of cystine in the body. The increased concentration of lysine in some of the subjects could have been due to the relatively high level of this amino acid in the preflight diet. At the end of the 5th day on a low-calorie diet, we demonstrated a decrease in concentration of 10 amino acids in the subjects' plasma: lysine, methionine, phenylalanine, histidine, arginine, glutamic acid, proline, alanine, cystine and tyrosine. The levels of three amino acids (threonine, valine, aspartic acid) showed virtually no change, whereas the concentration of four amino acids (isoleucine, leucine, serine, glycine) even increased somewhat. The levels of most amino acids in plasma remained within the "normal range" given in BME [19]. Cystine and aspartic acid were an exception, as in the preflight period, as well as methionine and arginine in some subjects due to the decrease in these two amino acids during the period on the low-calorie diet. The reliable decline in concentration of plasma lysine merits special attention; in the opinion of some authors this is a sign of development of protein deficiency [21]. It should also be noted that, by the end of the 5th day, we failed to observe an increase in levels of most amino acids actively involved in gluoneogenetic processes when there is insufficient intake of carbohydrates with food or a decrease in their mobile endogenous supply: alanine, glutamic and aspartic acids, threonine, valine, histidine, arginine, proline, cystine [22]. True, the concentration of glucoplastic glycine and serine still increased. Evidently, there was moderate use by the body of amino acids during this period for purposes of gluconeogenesis.

Table 3. Free amino acid content of blood plasma in subjects kept on a diet consisting only of chocolate for 5 days (n = 7) M±m

AMINO ACIDS	CONCENTRATION, MG%	
	FASTING 0800 HOURS FIRST DAY	FASTING 0800 HOURS FIFTH DAY
ESSENTIAL:		
LYSINE	4,13±0,11	2,57±0,13**
THREONINE	1,89±0,09	1,87±0,06
VALINE	2,25±0,11	2,25±0,09
METHIONINE	0,39±0,08	0,28±0,06
ISOLEUCINE	0,81±0,12	0,93±0,01
LEUCINE	1,40±0,10	1,81±0,09
PHENYLALANINE	0,78±0,06	0,66±0,04
NONESSENTIAL:		
HISTIDINE	1,44±0,07	1,19±0,10
ARGININE	1,30±0,12	0,97±0,10
ASPARTIC ACID	0,12±0,06	0,10±0,06
SERINE	1,30±0,11	1,62±0,08
GLUTAMIC ACID	0,86±0,14	0,81±0,10
PROLINE	2,14±0,16	1,84±0,07
GLYCINE	1,17±0,13	1,24±0,08
ALANINE	3,01±0,07	2,94±0,09
CYSTINE	0,77±0,10	0,62±0,12
TYROSINE	0,94±0,14	0,86±0,09
TOTAL AMINO ACIDS	24,7±0,10	22,56±0,08**
TOTAL ESSENTIAL (E)	11,65±0,09	10,37±0,06**
TOTAL NONESSENTIAL (N)	13,05±0,11	12,19±0,08*
E/N RATIO	0,89±0,04	0,85±0,02

* $P<0,05$; ** $P<0,01$.

Total amino acids, as well as total essential and nonessential amino acids in plasma diminished reliably in the subjects by the end of the 5th day. The ratio of essential to nonessential amino acids merely presented a tendency toward decline, due to the relatively more intesive decrease in concentration of essential amino acids than nonessential ones.

Thus, the dynamics of amino acid levels in plasma warrant the conclusion that there is only the initial stage of development of protein deficiency during a 5-day period of low-calorie nutrition using chocolate.

Table 4 lists the results of assays of total nitrogen excretion in urine before, during and after the emergency diet. In the base period, when the subjects were on the usual diet, nitrogen excretion was at the level of 16.02±0.23 g/day, which is indicative of rather high supply of protein in the body due to the diet. On the first day of the emergency diet, however, there was substantialy decrease in total nitrogen excretion, although the subjects received 44.5 g protein per day with the preflight breakfast (20 g chocolate).

Table 4. Total nitrogen excretion in 24-h urine before, during and after using low-calorie emergency diet consisting of chocolate (in grams)

No	SUBJECT	DAY ON USUAL DIET		DAY ON LOW-CALORIE EMERGENCY RATIONS						DAY AFTER EMERGENCY RATIONS		
										REHABILITATION DIET		USUAL DIET
		1	2	1	2	3	1—3	4	5	1—5	3	5
1	P-YEV	15,55	15,44	12,52	12,42	12,30	37,24	10,76	11,42	59,42	15,05	12,97
2	L-IY	16,75	16,90	12,90	11,21	10,83	34,94	10,39	10,17	55,50	12,78	14,74
3	T-KO	15,01	16,89	12,95	10,61	12,09	35,65	10,04	9,62	55,31	12,54	13,01
4	KH-OV	13,76	15,23	12,34	11,57	12,30	36,21	11,22	10,17	57,60	15,40	14,85
5	L-ICH	14,00	15,96	12,86	10,71	10,70	34,27	10,19	11,17	55,63	15,31	15,02
6	V-YETS	15,00	15,60	11,82	11,46	10,96	34,24	9,86	9,93	54,03	14,80	15,31
7	N OV	16,53	16,14	11,86	12,45	11,00	35,31	10,51	9,85	55,67	12,80	13,44
	M±m	15,23± 0,39	16,02± 0,23	12,46± 0,16	11,49± 0,25	11,45± 0,21	35,40± 0,42	10,42± 0,19	10,33± 0,25	56,16± 0,75	14,10± 0,40	14,05± 0,33

During the 2d-5th day on the emergency diet, as a result of using a low-calorie food allowance with low protein content, we observed in general a further decline in 24-h excretion of total nitrogen. This parameter constituted 10.33±0.25 g/day in 24-h urine specimens on the 5th day. Daily intake of nitrogen with chocolate averaged 0.85 g/day. Total nitrogen excretion in urine constituted 56.16±0.75 g over a 5-day period, while intake constituted about 10.53 g (counting the emergency rations and preflight breakfast). If we consider that extrarenal loss of total nitrogen when on a protein-free diet is 17 mg/kg body weight [23], in 5 days it should have constituted a mean of 6.42±0.14 g for the group of subjects. Consequently, the negative nitrogen balance constituted 52.10±0.72 g in 5 days. With average nitrogen content of the body of 1000 g, loss thereof in 5 days constituted 5.2%, which is far from the critical 50% loss.

After terminating the emergency diet and with change to a usual diet, total nitrogen excretion in urine started to increase on the very first day. On the 5th day, this parameter virtually reached the base level. All this is indicative of the minor change in nitrogen metabolism during a 5-day period on an emergency diet, as well as of the possibility of rapid restoration of protein metabolism after discontinuing emergency rations.

Assays of excretion in urine of K, Na, P and Cl revealed, for all subjects in general, a decrease in elimination of these macroelements for 5 days, and it was particularly noticeable on the 2d, 3d and 4th days. As compared to excretion when on a usual diet, the greatest decline was referable to elimination of Na and Cl, due to the change to a virtually salt-free diet. When on the usual diet, Na excretion in the subjects was at 4759±940 mg/day. In 1 day on the emergency diet, Na excretion dropped to 2394±218 mg/day;

on the 2d day it dropped to 956±100 mg/day, on the 3d to 606±139 mg/day, on the 4th to 460±80 mg/day and on the 5th to 364±76 mg/day. On the usual diet, Cl excretion in urine averaged 8107±1181 mg/day. On the 1st day of the emergency diet, this parameter dropped to 5591±502 mg/day, on the 2d to 2442±353 mg/day, on the 3d to 1387±180 mg/day, on the 4th to 970±109 mg/day and on the 5th to 863±159 mg/day. Na and Cl excretion on the 5th day differed little from the 4th, and this is apparently attributable to greater retention of these macroelements in the kidneys due to the danger of desalinization of the body. K excretion also diminished on the first days, but not as intensively. On the first day of emergency rations, the average decrease in K excretion for the group of subjects was not significant and remained in the normal range, 2108±155 mg/day. On the 2d day it dropped to 1569±95 mg/day, on the 3d to 1274±190 mg/day, on the 4th to 796±72 mg/day, which was already below the adopted physiological standard. On the 5th day, K excretion even increased, to 954±146 mg/day, which was somewhat higher than on the 4th day but lower than on the 3d. Such dynamics of K excretion could be attributable to stress reactions. P excretion when on ordinary diet constituted an average of 935±92 mg/day, i.e., it was in the range of the physiological norm (800-1200 mg/day) [16]. With the change to emergency rations, there was a decrease in P excretion in urine: to 753±102 mg/day on the 1st day, 655±93 mg/day on the 2d, 640±38 mg/day on the 3d, 635±41 mg/day on the 4th and 368±101 mg/day on the 5th day. The absence of increase in P excretion on the 5th day, as had occurred with K, is indicative of lack of marked stress at that period. Our data on excretion of macroelements in urine warrant the conclusion that some demineralization occurred with intake of 300 g chocolate as emergency rations for 5 days, particularly during the 2d and 3d days. Judging by the condition of the subjects, within the indicated time this demineralization did not elicit the distinct signs inherent in K, Na, Cl and P deficiency (weakness of muscles, seizures, etc.).

Evaluation of the subjects' EKG failed to demonstrate pathological changes. Heart rhythm remained sinusoid and regular. The time intervals of PQ, Q, QT remained within the normal range. There was no change in position of the axis of the heart. Amplitude characteristics of EKG waves did not undergo appreciable changes, with the exception of the T_2 wave, whose amplitude diminished somewhat. There was some widening of QT segment. These signs could be related to a change in electrolyte metabolism, but this requires confirmation. In general, mineral metabolism of K, Na, Cl and P can be evaluated as permissible, but it must be taken into consideration when organizing rehabilitation measures.

The subjects' general condition was rated satisfactory, according to medical observation during the period on the low-calorie diet.

Daily interrogation of the subjects and entries in their diaries [logs] enable us to describe the dynamics of their condition as follows. On the 1st day of emergency "survival," all of the subjects noted appearance of a sensation of hunger, already by their customary mealtime (in this case, dinner). This sensation of hunger did not cause severe anxiety and was abated after taking a few swallows of cold water. By the usual supper time, hunger became even stronger on the 1st day. The 20 g chocolate allocated for supper did not result in appreciable decrease in sensation of hunger, but did elicit more thirst. During the 2d-5th days, the subjects reported general weakness,

worsening of well-being, which progressed toward the end of the work day and diminished during sleep. Intake of the portions of chocolate briefly improved well-being, but appeasement of hunger was not complete or lasting. Intake of chocolate was usually associated with appearance of thirst and required additional intake of water. In spite of these changes in well-being, all of the subjects coped with their jobs without any particular difficulties.

Dynamometric evaluation of strength of hand muscles and "backbone [or supporting] strength" failed to reveal noticeable decrease in force parameters of muscles. By the end of the period of low-calorie nutrition, there was even a tendency toward greater strength of the hands with some decline of "backbone strength." During the period of usual nutrition, hand strengh constituted 59.1 ± 2.24 kg for the right hand and 56.9 ± 1.68 kg for the left, as the average for the group. On the 5th day of low-calorie rations, this parameter was 60.1 ± 2.1 kg for the right hand and 59.6 ± 1.96 for the left. "Backbone strength" reached an average of 128.9 ± 1.75 kg when on a usual diet, whereas on the 5th day of emergency rations it was 122 ± 5.6 kg. The strength of the hands constituted 59.2 ± 2.52 kg for the left hand and "backbone strength" was 127.8 ± 5.25 kg 5 days after the emergency diet. This is indicative of relatively good retention of strength parameters of muscles both during the period on a low-calorie diet and after its termination, with return to the usual diet.

These studies warrant the conclusion that a "survival" diet containing 300 g chocolate used in a temperate climate for 5 days, with energy expenditure of 3000-3200 kcal/day and limited water intake (1 ℓ/day) provides for preservation of relatively satisfactory well-being and work capacity under such conditions. At the same time, such a diet does not preclude development of hypoglycemic states as early as the 2d day on emergency rations, appearance of ketonemia and ketonuria from the 2d day on, deficiency and demineralization by the end of the 5th day. Moreover, intake of chocolate increases thirst and fluid requirements. All this does not allow us to consider chocolate as the "ideal" product for outfitting PES with a weight of 300 g, particularly when there is a limited supply of water.

We should also mention the great importance of the initial nutritional status to successful "survival" when using such low-calorie rations. For this reason, proper and wisely organized preflight nutrition should be considered an important hygienic factor, not only for safeguarding health and work capacity during flights, but to prolong "survival" time and preserve health under such conditions.

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EFFECT OF ENKEPHALIN ANALOGUE ON SOME DIGESTIVE FUNCTIONS DURING RESTRICTED PHYSICAL ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 1 Mar 82) pp 30-33

[Article by L. G. Goland-Ruvinova, V. A. Vinogradov and N. P. Goncharova]

[English abstract from source] Rats were exposed to 7-day hypokinesia and the effect of an enkephalin analog on the secretion of pepsin, amylase, the shape of the glycemic curve and the secretion of gastrointestinal hormones, gastric and insulin, was investigated. The hypokinetic exposure increased pepsin in the gastric mucosa and amylase in the pancreas, and decreased glycemia and insulin secretion. The analog normalized exo- and endocrine function of the pancreas and the shape of the glycemic curve.

[Text] One of the principal problems of biology is human and animal adaptation to the environment [1]. The stress reaction and stress syndrome play a substantial role in adaptation of an organism. It has been found that there is gradual increase in intensity of the stress syndrome with recurrent stress situations. It is assumed that there are modulatory systems in the body that limit the stress syndrome and prevent development of stress-induced injuries [2]. The system of endogenous opioid peptides--enkephalins and endorphins--which have diverse effect on different endocrine levels of expression of stress reactions in the body [3], have attracted particular attention.

In the case of restricted motor activity (RMA) [hypokinesia], considerable changes occur in severla physiological systems, and the systems in the regulation of which endocrine mechanisms are largely involved are the first to react. One of these systems, whose function depends on the state of neural and hormonal regulators, is the gastrointestinal tract.

At the present time, certain patterns have been established for the functional changes in digestive organs under RMA conditions varying in duration [4, 5]. At different stages of exposure to this extreme stimulus, different changes take place in enzyme-secreting, absorption and peristaltic-evacuation processes in the gastrointestinal tract. At the early stages of RMA (up to 14 days), the demonstrated changes in digestive system functions are a reflection of nonspecific stress reactions in the body, related to activation of the sympathoadrenal system.

The interest in gastrointestinal manifestations of stress is also attributable to the fact that the role of endogenous opioids in physiology and pathology of the digestive tract is presently being investigated intensively. For this reason, we investigated the effect of a synthetic analogue of enkephalins (AE) on some changes in the gastrointestinal tract induced by RMA.

Methods

We studied the effect of enkephalins on gastrointestinal tract functions on albino male rats weighing 180-200 g submitted to 7-day RMA. RMA was created by immobilizing the animals rigidly in special box-cages.

We assayed pepsin level in a homogenate of the gastric mucosa and pepsinogen level in blood [6]. Amylase activity was examined in a homogenate of pancreatic tissue and blood [7]. Concurrently, we studied the glycemic curve in response to a glucose load given by mouth. Blood glucose level was assayed on a fasting stomach and after a carbohydrate load for 2 h by the glucose oxidase method [8]. Blood serum insulin and gastrin concentrations were assayed by the radioimmunological method using standard sets of Sorin (France) reagents, following the directions of this firm. Insulin concentration was expressed in microunits per milliliter and gastrin in pg/mℓ.

AE was given to a group of animals during RMA, twice a day, in a dosage of 50 μg/kg daily. Saline was injected on an analogous schedule to control groups of animals--vivarium control and RMA.

The results of the studies were processed by the method of variational statistics, using the t criterion. Significance levels of less than 0.05 were considered reliable.

Results and Discussion

RMA (7 days) elicited a reliable increase (see Table) in pepsin activity in the gastric mucosa to 0.74±0.077 U, as compared to the vivarium control (0.4±0.07 U; $P<0.001$). At the same time there was insignificant elevation of blood pepsinogen level to 5.1±0.48 U (4.24±0.38 U in the control; $P>0.1$). Injection of AE to the RMA group of animals increased pepsin activity in the gastric mucosa even more, to 1.2±0.1 U. This was associated with reliable increase in pepsinogen incretion to 6.56±0.58 U, as compared to the vivarium control (4.24±0.38 U; $P<0.01$).

RMA led to reliable increase in amylase activity in pancreatic tissue to $214.6\pm54.3 \cdot 10^6$ U, as compared to $48.4\pm7.85 \cdot 10^6$ U in the vivarium control ($P<0.001$). However, incretion of this enzyme underwent virtually no change. Injection of AE during RMA caused drastic decline of amylase activity in the pancreas, to $11.8\pm0.79 \cdot 10^6$ U, which was considerably lower than in the vivarium control. We also observed some decline of blood amylolytic activity.

Examination of the glycemic curve after a glucose load enabled us to assess both the process of glucose absorption in the gastrointestinal tract and condition of the endocrine systems.

Gastric and pancreatic enzymes (M±m)

ANIMAL GROUP	STATIST INDEX	BLOOD		GASTRIC MUCOSA	PANCREATIC TISSUE
		AMYLASE	PLASMA PEPSINOGEN	PEPSIN	AMYLASE
VIVARIUM CONTROL	*M*	11 030	4,24	0,4	48 400 000
	m	1 230	0,38	0,077	7 850 000
	n	7	8	9	9
7-DAY RMA	*M*	10 030	5,1	0,74	214 600 000
	m	1 770	0,48	0,077	54 300 000
	n	8	8	9	9
	P	>0,5	>0,1	<0,01	<0,001
7-DAY RMA + TETRAPEPTIDE	*M*	8 966	6,56	1,2	11 885 111
	m	805	0,58	0,1	796 000
	n	8	8	9	9
	P	>0,1	<0,01	<0,001	<0,001

In vivarium control animals, maximum glycemia was observed 30 min after the glucose load; blood glucose level reached 7.13±1.07 mmol, as compared to the base level (3.48±0.11 mmol). After 2.5 h, blood glucose content was 1.8±0.19 mmol, which is indicative of adequate utilization by body tissues. With RMA, glucose level in blood dropped to 2.47±0.05 mmol (versus 3.48±0.11 mmol in the control; $P<0.001$). There was reliable decrease in glycemia 30 min after the carbohydrate load. However, 1.5 h after the load, unlike the vivarium control, glucose level was above the base and reliably higher than in the control. In general, the glycemic curve as lower after RMA, and it was more protracted than in the vivarium control. There was a decrease to almost one-half in coefficient of glycemia with RMA.

After giving animals AE, we demonstrated a higher glycemic curve--base glucose level rose to 3.48±0.13 mmol (versus 3.48±0.11 mmol in the vivarium control); after the carbohydrate load the maximum level of glycemia constituted 4.01±0.59, although it had shifted by the 90th min after the load. However, glucose increment was analogous in the RMA group of animals not given AE.

After RMA, we observed reliable depression of blood insulin content to 22.4±1.43 μU/mℓ, as compared to the vivarium control (37.2 ± 3.57 μU/mℓ; $P<0.001$).

AE caused insulin level in blood to rise to 29.9±2.3 μU/mℓ, which is virtually the same as in the vivarium control.

Analysis of gastrin secretion after 7-day RMA failed to demonstrate any changes whatsoever in level of this hormone in blood. Injection of AE to the group of animals with RMA also failed to have any effect on blood gastrin level.

Thus, with 7-day RMA, we demonstrated changes in enzyme secretion, manifested by increase in pepsin and amylase activity in glands that produce them. However, the blood levels of these enzymes showed virtually no change. This correlation between accumulation of enzymes and their secretion into blood is indicative of a primary reaction in the gastrointestinal tract. Analogous changes with regard to direction, which were transient, had also been observed following short-term spaceflights [5].

After prolonged RMA, along with intensification of production of digestive hydrolases, there was an increase in incretion of these enzymes [9]. In view of the fact that the early stages of RMA are characterized by marked activation of the adrenosympathetic system [10], as well as influence of this system on enzyme secreting processes in the gastrointestinal tract, the processes demonstrated during 7-day RMA could be interpreted as a reflection of a nonspecific stress reaction in the organism.

One of the manifestations of RMA was diminished absorption of glucose in the gastrointestinal tract, as evidenced by maximum depression of its concentration in blood 30 min after the carbohydrate load--a period of time related to the process of absorption of glucose in the gastrointestinal tract [11]. Subsequently, the nature of the glycemic curve with RMA was indicative of some glucose deficiency. There was a decrease in insulin concentration also, which is probably a compensatory reaction to lower glucose content in blood serum.

In this investigation, we tested the effect of an enkephalin analogue--Tyr-D-Ala-Gly-Phe NH_2 tetrapeptide--on the above-listed RMA-related changes. This peptide has a typical spectrum of biological activity inherent in endogenous opioid peptides and narcotic analgesics. In particular, intravenous injection of this analogue elicits analgesio. At the same time, we used very small doses of the analogue (50 μg/kg), which were 100 times lower than analgesic doses [12]. Nevertheless, injection of endogenous opioids in such amounts modifies appreciable behavioral reactions of animals and has a protective effect on the duodenal mucosa in experiments where ulcers were produced [13].

The demonstrated normalization of most RMA-related changes in carbohydrate metabolism could be attributed to the nonspecific antistressor effect of endogenous opiates, which play a modulating role with regard to secretion of a number of hormones very actively involved in formation of the stress syndrome [3]. Our data are indicative of normalization of the glycemic curve, concentration of insulin in blood, amylase level in blood and pancreatic tissue.

Injection of the enkephalin analogue to rats under RMA conditions averted development of RMA-related changes in carbohydrate metabolism and secretion of amylolytic enzyme by the pancreas. At the same time, we were impressed by the elevation of pepsinogen level, both in tissue of the gastric mucosa and blood. At the present time, it is difficult to explain this rise of pepsinogen level, but it can be assumed that it is related to some decrease in secretion of this enzyme into the gastric lumen. V. G. Smagina et al. [14] submit data on the anti-ulcer effect of the same AE, which is an indirect indication of this possibility. The anti-ulcer effect of this peptide is probably largely related to diminished activity of the acid-peptic factor. It can be assumed that this is associated with appreciable change in the role of increted pepsinogen in general homeostatic reactions of the body [15].

In our opinion, our findings should draw attention to the antistress protective effect of endogenous opioid peptides and their synthetic analogues.

The demonstrated patterns require further in-depth investigation, since they may be of substantial relevance to prophylaxis and prevention of various changes in the body related to stress, in particular with RMA.

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INVESTIGATION OF PHASE STRUCTURE OF CARDIAC CYCLE DURING LBNP TESTS IN LONG-TERM (140-185-DAY) SPACEFLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 10 Feb 82) pp 33-37

[Article by A. D. Yegorov and A. P. Polyakova]

[English abstract from source] Before and during prolonged space flights changes of systolic time intervals in response to LBNP tests were qualitatively similar and corresponded to the syndrome of myocardial hypodynamics due to insufficient venous return. However, the level of the changes and their contribution to the cardiac cycle were different in flight and on the ground. Greater changes in systolic time intervals seen in flight may be attributed to larger blood shifts to the abdomen and legs.

[Text] Extensive use is made of the test involving application of negative pressure to the lower part of the body (OBNP) in medical monitoring of the condition of crews during long-term spaceflights [1-10]. This test is an analogue of an orthostatic test (under the effect of LBNP blood shifts to vessels in the lower part of the body), and it is used both to assess the current state of the crew in flight and to predict orthostatic stability in the postflight period.

Studies of phase structure of the cardiac cycle during LBNP tests during missions aboard the Soviet orbital stations, Salyut-1, Salyut-3, Salyut-4 and Salyut-5 [1, 5, 11] revealed a number of changes in cardiac function. Considering the relatively short duration of the above-mentioned flights (up to 2 months) and inadequate volume of tests, it was deemed expedient to continue the study of phase structure of the cardiac cycle using the LBNP test during flights of longer duration aboard the Salyut-6--Soyuz orbital complex.

Methods

Phase structure of the left ventricular systole was examined by the method of kinetocardiography using Polynome-2M ["Polinom"] equipment aboard the orbital station [2-5, 12]. We used a piezoceramic sensor, the receiving part of which (rubber capsule 4×6 cm in size, filled with paralon [typo for porolon--plastic?]) was placed in the region of the apical beat of the heart. The recorded data were

transmitted via telemetry channels to the ground. The Chibis pneumovacuum gear, in the form of crimped trousers, installed on the station was used for the LBNP functional test. With this test, two-step rarefaction was produced as follows: -25 mm Hg for 2 min, -35 mm Hg for 3 min.

The kinetocardiograms were interpreted before and after rarefaction of -35 mm Hg by the method described by L. B. Andreyev and N. B. Andreyeva [13]. We measured the following parameters: duration of cardiac cycle (CC), mechanical systole (MS), isometric contraction (IC) phase and sphygmic [expulsion] period (SP). In addition, we calculated the ratio of actual values for MS and SP to the nominal ones (nominal values were determined using the formulas of V. L. Karpman [14]), as well as derivative parameters--index of myocardial tension (IMT), intrasystolic index (ISI) and ratio of duration of IC phase to SP (interphase coefficient K). We analyzed changes in the parameters at rarefaction of - 35 mm Hg, as compared to average values obtained 3 min before the test. We also compared data during rarefaction of -35 mm Hg, obtained in flight, to analogous preflight values. The data were submitted to statistical processing by the method of variance analysis [15] followed by comparison of mean values (monthly) obtained in flight to preflight parameters.

The tests were conducted on commanders and flight engineers referable to the main crews of the Salyut-6--Soyuz orbital complexes who participated in the second (CDR-2, FLE-2), third (CDR-3, FLE-3) and fourth (CDR-4, FLE-4) missions lasting 140, 175 and 185 days. In all, we conducted 3-6 tests on each cosmonaut before and during the flights.

Results and Discussion

General patterns of changes in parameters studied

Variance analysis revealed that flight duration and interaction of LBNP test had a statistically significant ($P<0.05$) effect on the parameters of phase structure of the left ventricular systole.

The most common patterns of change in phase structure of the left ventricular systole before and during the flight with rarefaction (as compared to pretest data) were: shortening of CC and MS; longer IC, IMT and K phases; diminished SP with concurrent negligible increase in ratio of actual values for this parameter to nominal; decrease in value of ISI.

The demonstrated patterns of change in CC during LBNP coincided in direction with the changes observed in orthostatic tests [16]. This is apparently attributable to the fact that the LBNP test, like the passive orthostatic test, elicits a shift [of blood] to vessels in the lower half of the body, due to the larger capacity of the venous bed and its ability to dilate under the effect of hydrostatic blood pressure [17, 18]. As a result, there is deposition of blood in the decompression zone under the effect of LBNP, which is proportional, according to the data of Guyton [17], to the extensibility of vascular walls. LBNP apparently diminishes venous return and delivery of blood to the heart and cardiopulmonary region, which leads not only to change in the hemodynamic situation, but appearance of a number of reflex reactions. The decrease in force of myocardial contraction due to decreased venous return and blood supply to the

heart was associated with increased duration of IC, IMT and K during the LBNP test.

The decrease in stroke volume, which is observed during LBNP tests [4-6, 8, 9], is due to diminished venous return and apparently causes shortening of SP with concurrent increase in ratio of its actual value to nominal.

Thus, we observe development of a phase syndrome of functional myocardial hypodynamia due to volumetric underloading of the heart under the effect of applying "negative" pressure.

Dynamics of tested parameters in flight

Comprehensive analysis enabled us to detect a number of distinctions referable to dynamics of parameters of phase structure of CC in flight during LBNP tests with -35 mm Hg.

We found that there was greater shortening of the CC during rarefaction in 5 out of 6 cosmonauts than before the flight, whereas in CDR-3 it exceeded preflight data. Mean duration of MS in flight, during the LBNP test, was shorter than the average values in the preflight period with the same level of rarefaction, in 5 out 6 cosmonauts.

Extension of the IC phase, which was observed in flight during LBNP in all 6 cosmonauts, was more marked than preflight. In 4 cosmonauts, this parameter had a tendency toward increase as a function of flight duration, and in 2 it had a tendency toward decrease. Moreover, the increment of this parameter during inflight LBNP was more marked than before the flight, in relation to the mean values prior to the test (Figure 1).

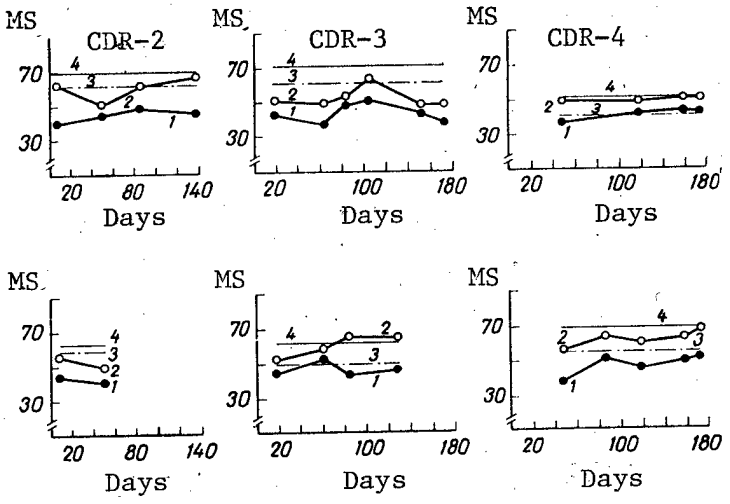

Figure 1. Dynamics of mean duration of IC phase of left ventricle in crew members during LBNP in 140-, 175- and 185-day spaceflights

Here and in Figure 2:

1 and 2) before test and with rarefaction of -35 mm Hg during flight, respectively

3, 4) same in preflight period

Duration of SP diminished in all cosmonauts during LBNP, and in most cases the degree of shortening was more marked in flight than preflight. Shortening of SP in relation to pretest level was more marked in flight than preflight (Figure 2). The ratio of actual SP to nominal was lower in flight in a number of instances than the corresponding parameter.

ISI was higher during LBNP in flight in 4 cosmonauts and lower in 2 than in the preflight period.

K also was usually lower than the preflight value during inflight rarefaction in 5 cosmonauts and was higher in only one of them.

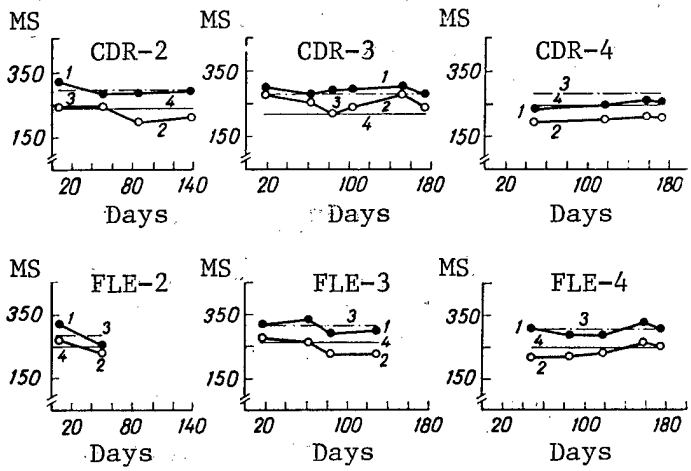

Figure 2. Dynamics of mean duration of left ventricular SP in crew members during LBNP in 140-, 175- and 185-day spaceflights

IMT during inflight LBNP was tested in 4 cosmonauts. In most tests, this parameter was lower than the corresponding preflight level in 3 of them and higher in the fourth. As compared to mean pretest values, the increment of IMT and K during inflight LBNP was more marked than before the flight.

Thus, during the inflight LBNP test (as compared to the preflight period), we observed the following distinctive changes in parameters of phase structure of the left ventricular systole: more marked increment in duration of IC, IMT and K phases, and less marked increase in absolute values of these parameters; more marked decrease in absolute values of SP and its increment (in relation to levels before rarefaction), as well as in absolute ISI in a number of instances.

It may be assumed that the LBNP test in weightlessness elicits greater migration of blood from the chest than on the ground (the initial blood volume in the chest is probably increased in the chest, in spite of the decrease in total circulating blood volume) to abdominal organs and the lower extremities in the decompression zone [10, 19]. This is manifsted by an increase in volume of the lower leg in flight under the effect of LBNP [10]. Most of the enlargement of the lower leg in flight occurs within the first 2 min of LBNP (-8 and -16 mm Hg), which is indicative of existence of a zone free extensibility of veins: the veins acquire a flattened or ellipsoid shape, instead of round, due to the

low transmural pressure [20]. Hence, venous return could decrease even more in weightlessness than on the ground under analogous conditions, and this leads to greater decrease in stroke volume. Evidently, the drastic decrease in blood volume in the cardiopulmonary region causes reflex increase in activity of the vasomotor center with intensification of adrenergic influences [21, 22]. This apparently explains the more marked changes in cardiac function during the inflight LBNP tests, including more marked increase in heart rate and peripheral resistance [4-9].

In turn, these phenomena very probably cause considerably greater decrease in SP and its increment (in relation to prerarefaction levels) and, in a number of cases, absolute ISI. Thus, the distinctions of changes in phase structure of the CC under the effect of inflight LBNP could be related to the greater migration of blood under these conditions (as compared to the ground) to the abdominal cavity and legs during decompression.

It should be noted that we failed to demonstrate progressive accentuation of changes in parameters of cardiac activity during inflight functional tests with LBNP. This indicates that the adaptive reactions and reserve capabilities of the body provide, during flights lasting up to 6 months and with the selected modes of LBNP tests, for rather good regulation of cardiac function and maintenance of relatively constant functional level.

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EFFECT OF IMMERSION IN WATER AS A WEIGHTLESSNESS MODEL ON LUNG CLOSING VOLUMES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 17 Feb 82) pp 37-40

[Article by M. A. Tikhonov, A. V. Kondakov, N. M. Asyamolova and M. Yu. Volkov]

[English abstract from source] The effect of 7-day water immersion combined at night with head-down (6°) tilting on the volumes of lung expiratory closing was examined in 6 healthy male test subjects aged 25-35. During immersion they showed, along with a stable reduction of the lung vital and functional residual capacity (by 4.2 and 14.8%, respectively), an increase in the fraction parameters of the expiratory closing volumes. The increase in the closing volume (up to 40%) ($P<0.05$) was particularly distinct on immersion day 2. Subsequent changes indicated gradual recovery of the closing volumes and a decline in regional nonuniformity of lung ventilation. The time-course variations in the closing volumes may be attributed to an increase in the intrapulmonary blood volume at the early stage of adaptation to immersion and to a decrease in the nonuniformity of the ventilation-perfusion ratios.

[Text] Many works have been published to date indicative of marked gravitational effects on regional distribution of pulmonary blood flow and ventilation [1, 2]. In particular, with simulation of physiological effects of weightlessness by the water immersion method, the following findings were made: decreased residual functional volume of the lungs (RFV), increased resistance of airways and decreased elasticity of the lungs, which is apparently attributable to the distinctions of respiratory biomechanics in the immersion medium, redistribution of circulating blood and increase in its intrathoracic volume [3].

Since diminished stretchibility [elasticity] of the lungs, hypervolume and static phenomena in the peribronchial vascular system are associated with compression and impaired patency of fine peripheral airways [4], we could expect in weightlessness more marked regional nonuniformity of pulmonary ventilation, which is instrumental in alveolar shunting of nonoxygenated venous blood and impairing exchange of gases.

However, this hypothesis requires experimental verification. For this reason, our work involved investigation of the distinctions of regional ventilation of the lungs with simulation of weightlessness by means of immersion in water and

placing the body in antiorthostatic [head down] position, with examination of the dynamics of expiratory closing of airways (ECA).

Methods

These studies were conducted with 6 healthy males 22-28 years of age, under conditions of 7-day water immersion, which was combined at night with anti-orthostatic hypodynamia (AOH)--6°.

We determined static lung volumes and ECA parameters in the subjects before submersion in the immersion medium, 2 h after immersion and then every 24 h of immersion.

Vital lung capacity (VC) and its constituents--inspiratory reserve volume (IRV), expiratory reserve volume (ERV) and respiratory volume (RV)--were determined by means of a Godart water spirograph, RFV by means of a kataferometer [typo for katathermometer?] and digital computer from the spirograph with the helium dilution method.

ECA (constriction or complete closer of fine bronchi in expiration) was studied by the bolus method [5] using helium as test gas.

The existing methods of studying ECA are based on demonstration of the so-called 4th phase of expiratory curve of test gas. The volume corresponding to the 4th phase, as determined by the expiration spirogram, constitutes the volume of lung closure. As a rule, the smoothing of regional differences in pulmonary ventilation of healthy people makes it difficult to detect the lung closing volume (LCV). For this reason, we made some changes in the usual method of measuring ECA (Figure 1). We added a spring-loaded valve *2* with resistance R_i = 30 mm water$\cdot\ell^{-1}\cdot$s into the inspiration line and additional resistance *3* R_e = 25 mm water$\cdot\ell^{-1}\cdot$s to the expiration line (to stabilize its volumetric velocity), in order to demonstrate better the 4th phase of the expiratory curve.

We determined the following ECA parameters by means of synchronous recording on a two-coordinate Rickem-Denchi recorder of expiratory concentration of helium and expiration volume: LCV--the part of VC from the start of ECA to the level of residual volume (RV), lung closing capacity (LCC)--sum of LCV and RV, reserve RFV (RRFV)--the part of VC from level of calm expiration to start of ECA.

Results and Discussion

The data characterizing dynamics of measurement of static lung volumes and ECA parameters during 7-day immersion are listed in the Table.

After submersion of the subjects in water, we demonstrated a decrease in VC and RFV by an average of 4.2 and 14.8%, respectively. In all cases, this decline was attributable to marked (average of 31.3%) restriction of ERV. At the same time, there was unreliable ($P<0.05$) decrease in total lung capacity (TLC). These changes in static lung volums persisted at about the same level for all 7 days of immersion.

Dynamics of static lung volumes and ECA parameters (in liters) during 7-day immersion (M±m; n = 6)

DAY OF STUDY	IRV	ERV	VC	RV	RFV	RV	TLC	LCV	LCC
BACK-GROUND	2,6±0,22	1,6±0,22	4,8±0,22	0,633±0,055	2,7±0,09	1,1±0,14	5,9±0,12	0,43±0,05	1,5±0,15
1	2,9±0,15	1,1±0,13*	4,6±0,17	0,650±0,050	2,3±0,10*	1,2±0,09	5,8±0,09	0,93±0,10*	2,1±0,14*
2	2,9±0,15	0,8±0,06*	4,3±0,16	0,600±0,051	2,1±0,10*	1,3±0,08	5,6±0,14	0,98±0,14*	2,3±0,13*
3	2,9±0,19	0,9±0,07*	4,4±0,25	0,516±0,065	2,3±0,09*	1,3±0,11	5,7±0,21	0,86±0,12*	2,1±0,14*
4	2,9±0,16	0,9±0,09*	4,5±0,17	0,653±0,061	2,2±0,06*	1,3±0,06	5,8±0,13	0,67±0,09	2,0±0,11
5	3,0±0,19	0,9±0,10*	4,5±0,15	0,533±0,061	2,3±0,06*	1,4±0,08	5,9±0,17	0,62±0,08	2,0±0,15
6	3,0±0,19	0,8±0,13*	4,4±0,18	0,583±0,047	2,4±0,10	1,5±0,11	5,9±0,18	0,48±0,05	1,9±0,15

*Differences from background are reliable with P<0.05.

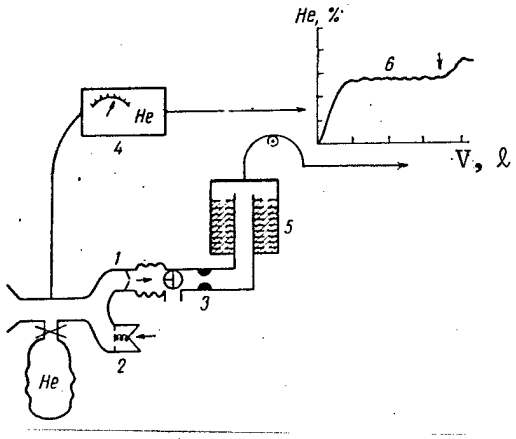

Figure 1.
System of studying lung closing volumes with bolus method. Arrowhead shows start of 4th phase of ECA
1) mouthpiece with valve box
2) wire-loaded inspiration valve
3) resistance in expiration line
4) kataferometer
5) spirograph
6) curve of expiratory concentration of helium

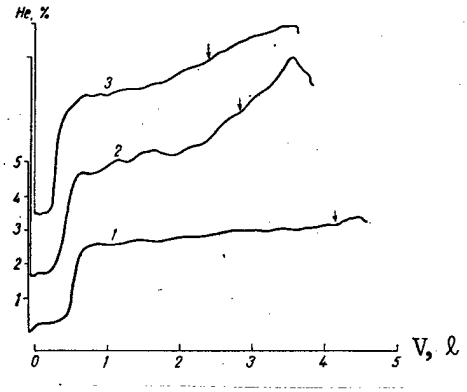

Figure 2.
Dynamics of expiratory concentration of helium in one of the subjects
1) base state
2,3) after 2 h and 2 days, respectively, of immersion

Hydrostatic pressure of fluid on the body submerged in it should be considered the chief cause of changes in static lung volumes. This pressure disrupts equilibrium between gravity and elastic forces of the lungs and chest which determine the level of RFV, and it reduces lung volume. Moreover, the presence of transthoracic pressure gradient, as a result of which the subject appears to be breathing under constant negative pressure, is instrumental in influx of blood to the lungs and increase of its intrathoracic volume. Both factors, i.e., decrease in lung volume and increase in central blood volume, in turn alter the elastic properties of the lungs and resistance of airways.

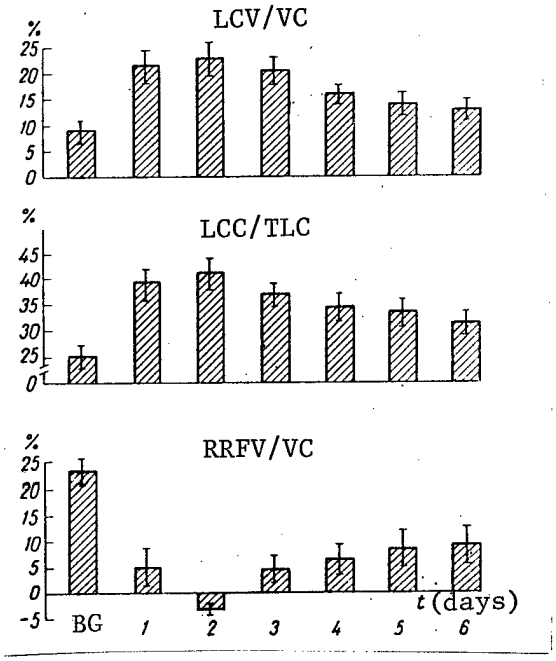

Figure 3.
Dynamics of partial parameters of expiratory airway closure during 7-day immersion
BG) background

This is indicated by the observed changes in LCV in the subjects during immersion (see Table and Figure 2).

According to the data in Figure 2, LCV constituted 0.39 ℓ in one of the subjects and increased to 0.95 and 1.1 ℓ after 2 h and 2 days of immersion, respectively. The concurrently observed increase in angle of inclination of the alveolar "plateau" of expiratory concentration of helium is indicative of deterioration of the process of intrapulmonary mixing of gases. The increase in LCV and LCC during immersion in water, by 116 and 40%, respectively, is indicative mainly of development of peripheral bronchiolar obstruction, which confirms our working hypothesis. Special mention should be made of the drastic elevation of ECA constituent parameters in the overall structure of lung volumes.

We know that the sooner ECA occurs in the process of expiration, the poorer is ventilation of the lungs, the greater the admixture of venous blood in arterial blood and the more marked hypoxemia is present [6]. The so-caled RFV reserve (difference between RFV and LCC) is the main criterion of ECA for evaluation of ventilation-perfusion relations in the lungs. When LCC is greater than RFV, there are poorly ventilated zones due to ECA in the lungs, even during calm breathing, and part of the unoxygenated venous blood is shunted into the arterial system.

In our studies, we demonstrated a decrease in RRFV by an average from 1.3 in the base state to disappearance after 2 days of immersion. There were even more marked changes in ratio of RRFV to VC (RRFV/VC), which dropped from 25 to 4% ($P<0.01$) already on the 1st day.

Apparently, we can interpret the ECA changes observed at the start of immersion as a manifestation of regional obstruction of peripheral airways, which leads to increase in partial lung volumes with impaired ventilation.

It is known that in the case of laminar air flow, which is prevalent in the bronchioles, their resistance, according to the law of Poiseuille, is proportional to volumetric flow velocity, length of airways and dynamic viscosity of air. Other conditions being equal, it is inversely proportional to the fourth power of the airway radius. For this reason, even an insignificant decrease in cross-section area of the bronchi with decrease in lung volume causes an appreciable increase in resistance of the airways. The stasis of blood in peribronchial vessels is also instrumental in reduction of their lumen.

The dynamics of ECA parameters during 7-day immersion (see Table and Figure 3) speak in favor of the last circumstance. The most distinct increase in partial

ECA parameters and decrease in RRFV were observed on the 2d day of immersion, while subsequent changes were indicative of a tendency toward recovery, with stable decrease in lung volume.

These dynamics of ECA parameters could be due to triggering of neurohumoral reactions (Henry-Gauer reflex), which cause reduction of central blood volume and alleviate the conditions of pulmonary hemodynamics.

By extrapolating the data obtained on change in ECA during immersion to weightlessness, we should expect that the redistribution of blood and increase in its intrapulmonary volume at the early stage of adaptation to weightlessness are also associated with regional disturbances referable to ventilation-perfusion ratios in the lungs, the severity of which regresses as the adaptation process develops.

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EXERCISE TOLERANCE FOLLOWING WATER IMMERSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 4 Feb 82) pp 40-45

[Article by Ye. B. Shul'zhenko, K. I. Gogolev and S. M. Belyayev]

[English abstract from source] Before and after 24-hour water immersion test subjects performed a submaximal workload on a bicycle ergometer. Changes in their hematocrit, circulating plasma volume and fluid balance were compared with those during immersion. As a result, the test subjects were subdivided into two groups. For one group the workload was very hard; adaptation to immersion was accompanied by significant renal losses of fluid from the intra- and extravascular space. The bicycle ergometry test after immersion demonstrated a decrease of exercise tolerance combined with circulatory disorders. The other group showed a higher exercise tolerance; after immersion exercise tolerance remained high at the expense of the reserves that maintained optimal blood supply to the working muscles.

[Text] The development of cosmonauts poses more and more new problems, among which a special place is held by questions of assuring efficient performance by cosmonauts of various operations in weightlessness. For this reason, it is considered quite urgent to continue with investigations of physical work capacity of man as a property for adapting to the demands made by the environment of the muscular apparatus and systems that implement its activity [1]. Several authors [2, 3] have advanced the opinion that cardiovascular changes play the leading role in the genesis of changes in man's physical work capacity after simulating some of the effects of weightlessness.

Our objective here was to assess the reactions of the cardiorespiratory system to graded submaximum physical exercise before and after 3-day immersion, as compared to changes in level of hydration of the intravascular space.

Methods

We used water immersion ("dry" submersion method) as a model of weightlessness for 3 days [4]. A functional load of 100 W lasting 15 min was used as the exercise test. It was performed on a bicycle ergometer in supine position, with pedaling at the rate of 60±5 r/min. The tests were conducted on 7 male volunteers 25-32 years of age. In all instances, the bicycle ergometer test was conducted in the morning under close to basal metabolic conditions 24 h

prior to submersion (after staying in horizontal position for 1 h) and after immersion (10-15 min after exiting from tank). Before exercise, as well as during pedaling (8th and 15th min), we determine minute volume ($\dot{V}$), oxygen uptake ($\dot{V}_{O_2}$) and CO_2 output ($\dot{V}_{CO_2}$), minute volume of circulation (Q) by the rebreathing method, as well as systolic, mean and diastolic blood pressure by the tachooscillographic method. During the study, we recorded the EKG in the Neba leads to determine the heart rate (HR). We estimated stroke volume $\dot{Q}_S$, oxygen pulse (OP), coefficient of oxygen utilization (CU_{O_2}), cardiac load index (CLI--derived from HR and systolic pressure [5]) and total peripheral resistance of vessels (TPR) [6]. The methods have been described in greater detail previously [7].

We analyzed the hematocrit index (Hmt) before and after 3-day immersion [8], on the basis of which we estimated, stage by stage, the changes in circulating plasma volume. Blood for the tests was taken in the morning, on a fasting stomach, just prior to submersion in the tank (after spending 45-50 min in supine position) and at the end of the 3d day of immersion.

We determined the overall fluid balance for the immersion period, estimating the difference between fluid intake including the liquid portion of food and elimination through the kidneys (data of Ye. A. Aleksandrova).

Analysis of the results obtained from tests at all stages enabled us to make a distinction between two groups of subjects, the dynamics of $\dot{Q}$, $\dot{Q}_S$, HR and TPR in whom presented appreciable differences. The data were submitted to statistical processing both within and between groups, using Student's criterion.

Results and Discussion

Before immersion, there was virtually no differences between groups in the base values of the parameters studied. Hmt was the only exception, constituting 45.3% in the first group and 49.0% in the second ($P<0.1$).

During exercise before immersion, the study revealed that there was almost the same increment of HR in both groups of subjects in the 8th min of the test; however, the higher percentage of increase in $\dot{Q}_S$ in the first group of subjects led to greater increment of $\dot{Q}$ ($P<0.01$; see Table); the decline of TPR was reliably greater ($P<0.01$) in the second group. The hemodynamic change was associated with the same increase in $\dot{V}_{O_2}$ in both groups, but in the first group there was unreliable change in CU_{O_2} due to higher values for $\dot{V}$ and in the second group CU_{O_2} doubled ($P<0.01$) while $\dot{V}$ increment was less marked ($P<0.1$).

In the 15th min of the test, the differences between responses leveled off; however, the greater increment of HR in the first group caused persistance of difference in OP; the percentage of increase in CU_{O_2} in the second group of subjects was 2.5 times greater than in the first group ($P<0.001$).

A negative fluid balance was noted in all subjects during immersion, but it constituted 1615 mℓ ($P<0.001$) in the first group and 311 mℓ ($P<0.05$) in the second. Comparison of individual blood tests at the end of the immersion period revealed increase of Hmt (14.1% in the first group, $P<0.001$ and 6.4% in the second, $P<0.25$), which was indicative of decreased volume of intravascular fluid by 22.6% in the former case ($P<0.001$) and 11.7% in the latter ($P<0.25$).

Some parameters of cardiorespiratory system during graded physical load before (1) and after (2) immersion (M±m)

GROUP	TIME OF STUDY	HR/min		$\dot{Q}_s$, ml		$\dot{Q}$, l		TPR, dyne·s/cm^5		CLI, arbitrary units/10^2	
		1	2	1	2	1	2	1	2	1	2
FIRST (n=4)	AT REST	64,3±5,5	65,8±4,3	72,8±7,7	63,0±2,2	4,57±0,40	4,12±0,18	1645±62	1940±165	76±6,6	82±4,8
	EXERCISE: 8TH MIN	139,5±8,2	152,5±6,6	144,6±11,1	104,3±6,9	20,00±1,17	16,01±1,59	389±21	505±59	260±17,7	285±25,0
	15TH MIN	151,5±8,1	172,3±6,1	128,9±11,4	96,1±4,6	18,90±1,11	16,23±1,14	408±35	506±55	286±30,7	369±37,4
SECOND (n=3)	AT REST	58,7±4,7	55,7±4,3	83,9±6,4	87,4±4,0	4,86±0,14	4,86±0,41	1578±32	1453±46	66±3,6	61±6,5
	P		<0,2	<0,5	<0,01		<0,2		<0,05	<0,3	<0,05
	EXERCISE: 8TH MIN	119,7±10,2	115,0±6,5	117,5±11,2	145,8±5,4	13,80±0,37	17,07±0,45	556±29	498±28	193±3,35	182±4,70
	P	<0,2	<0,01	<0,2	<0,01	<0,01		<0,01		<0,1	<0,03
	15TH MIN	121,7±10,1	126,7±9,5	138,3±20,7	149,6±6,4	17,07±1,38	18,84±0,82	485±56	425±25	213±30,4	198±26,2
	P	<0,1	<0,01		<0,001	0,5	<0,25	<0,5	<0,25	<0,2	<0,02

GROUP	TIME OF STUDY	$\dot{V}$, l		$\dot{V}_{O_2}$, ml/kg·min		OP, ml/beat		CU_{O_2}, ml/l		$\dot{V}_{CO_2}$, ml/min	
		1	2	1	2	1	2	1	2	1	2
FIRST (n=4)	AT REST	7,37±1,82	5,80±0,77	2,4±0,5	2,0±0,3	2,7±0,6	2,2±0,4	22,7±4,2	21,6±1,1	199±40,9	139±20,7
	EXERCISE: 8TH MIN	46,90±5,09	45,10±7,77	21,7±5,4	18,1±2,5	10,5±1,7	7,9±1,0	29,3±6,7	27,3±4,3	1915±120,3	1307±368,6
	15TH MIN	45,13±1,76	40,90±10,06	23,6±2,6	19,3±5,3	11,1±0,9	7,8±1,2	32,3±3,3	30,4±2,6	1827±71,4	1485±373
SECOND (n=3)	AT REST	7,71±1,50	8,72±2,34	2,2±0,3	2,6±0,5	3,1±0,6	3,8±0,9	21,0±0,6	21,8±2,8	213±50,7	225±66,7
	P		<0,25		<0,5		<0,2				
	EXERCISE: 8TH MIN	32,57±3,35	37,17±4,70	20,0±3,8	18,9±3,3	13,3±1,3	13,0±1,7	43,5±4,5	36,0±5,1	1473±152,6	1480±102,9
	P<	0,1	0,5			0,5	0,05	0,2	0,25	0,1	
	15TH MIN	38,03±3,65	37,20±3,43	22,5±1,4	19,9±1,1	14,6±1,6	12,7±1,4	42,9±2,6	38,1±2,5	1705±54,8	1512±58
	P	<0,2		<0,5		<0,1	<0,05	<0,1	<0,1		

Key: P) reliability of difference in comparing parameters in the course of the study in different groups.

Analysis of hemodynamic data after immersion revealed that $\dot{Q}_S$ was reliably lower in the first group at rest than in the second group of subjects, while TPR and CLI were reliably higher. In addition, the first group of subjects presented a tendency toward prevalence of HR, which diminished difference $\dot{Q}$ and increased difference in OP, as compared to the corresponding values for the second group.

Exercise on the bicycle ergometer after immersion for 7 min elicited a 137.2% increase in HR of the first group, as compared to preimmersion level at rest, whereas in the second group of subjects this parameter constituted only 95.9% ($P<0.01$). This was associated with a 43.3% increase in $\dot{Q}_S$ in the first group of subjects and 73.8% increase in the second group ($P<0.01$); parameter $\dot{Q}$ increased by 3.5 times in both groups of subjects, but this increment was 20% less in the first group, in comparison to the dynamic background ($P<0.1$) and 23.7% greater in the second group ($P<0.001$). The percentile decline of TPR was the same, but there was a tendency toward decline, as compared to the dynamic background (29.8%) in the first group, and toward rise in the second group (10.4%).

$\dot{V}$ and CU_{O_2} did not change in the first group of subjects, as compared to background dynamics; in the second group, $\dot{V}$ increased by 14.1% ($P<0.5$) while CU_{O_2} declined (16.9%, $P<0.5$). This was associated with a tendency toward decline of $\dot{V}_{O_2}$ (16.6%) and $\dot{V}_{CO_2}$ (31.8%) in the first group, but with virtually no change in the second.

The results of examination at the end of the exercise test revealed that HR increased by 168% in the first group, versus 115.8% in the second ($P<0.01$), but the difference between $\dot{Q}_S$ values (32 and 78.3%, respectively, $P<0.002$) retained the previously demonstrated (8th min) nature of changes in $\dot{Q}$ (-14% in the first group, $P<0.25$; +10.4% in the second, $P<0.5$). TPR did not continue to change in the first group of subjects, but continued to drop in the second ($P<0.25$). At this stage of exercise, $\dot{V}_{O_2}$ increased to about the same extent, but CU_{O_2} was 33.9% above the initial level ($P<0.5$) in the first group and 81.4% higher in the second group ($P<0.01$).

Analysis of our results revealed that exercise on the bicycle ergometer led to increase in stroke and minute volumes of circulation, which provided for increasing muscular blood flow, minute volume of respiration and oxygen uptake, which were related to increased expenditure of energy, and decline of TPR. Such a reaction is indicative of adjustment of the cardiorespiratory system to the conditions under which muscular function led to considerable increase in effective vascular bed due to dilatation of precapillary resistive vessels [10]. In spite of the identical power of the test exercise, the magnitude of the responses before immersion differed in the two groups. In the first group of subjects, the early stage of exercise elicited a more substantial increase in minute volume of circulation ($P<0.1$), but increment in oxygen uptake was virtually the same in the two groups. This was associated with minimal change in coefficient of O_2 uptake in the first group and a 2-fold increase of this index in the second group ($P<0.25$). Evidently, such an effect was attributable to the difference between Hmt levels, which were lower in the first group. In the opinion of Folkov and Nil [10], the decrease in oxygen capacity of blood is greater than the increase in oxygen delivery due to intensification of blood flow when its viscosity diminishes with lower Hmt. In the first group of subjects, compensation also included a greater increment of minute respiratory volume ($P<0.1$).

For the first group, the exercise load was functionally more difficult to carry, since the percentile decline of TPR was greater ($P<0.1$). It is known that the degree of vasodilation of the vascular bed is proportional to intensity of a physical load [10]. Moreover, exercising by the first group of subjects was characterized by a tendency toward greater output of CO_2, as compared to O_2 uptake ($P<0.25$), which could be indicative of low work capacity [11].

Analysis of studies of fluid metabolism revealed that fluid loss through the kidneys during the immersion period was more than 5 times greater in the first group than the second ($P<0.001$). This was associated with less (by 1.8 times) decline in volume of intravascular fluid in the second group of subjects ($P<0.001$). Thus, if we compare the estimated decline in volume of circulating plasma (730 mℓ) and amount of renal fluid loss (1615 mℓ) in the first group, we can maintain that there was elimination of both intravascular and extravascular fluid (885 mℓ) during the immersion period. Renal loss was analogous to the extent of decline in intravascular volume in the second group of subjects.

In this regard, it is important to stress the difference in TPR dynamics after immersion. Thus, the first group of subjects presented a tendency toward increase and the second group, toward decrease, which probably led to different changes in correlation between precapillary and postcapillary resistance. The increase in TPR in the first group apparently elicited a change in the filtration process--absorption of fluid through the capillary wall in the direction of the latter [12, 13], which led to loss through the kidneys of fluid in the vascular and interstitial spaces. In the second group of subjects, TPR diminished, and this stimulated migration of some of the fluid into the extravascular space, causing a decrease in total circulating plasma and averting major fluid loss.

When working on the bicycle ergometer after immersion, the first group presented more significant HR increment (as compared to background dynamics) with substantial decrease in stroke volume ($P<0.02$). The hemodynamic changes were associated with a tendency toward decreased O_2 uptake and CO_2 output, whereas respiratory volume and CU_{O_2} differed little from background values. Such phenomena, together with the greater TPR during the exercise load, could indicate that part of the nutritive section of functioning muscles was not involved, due to functional inconsistency between effective volumes of circulating blood and "working" vascular stream. The decrease in circulating blood volume in this group occurred because of decrease in plasma during immersion, while replenishment of the deficient erythrocyte "carrier" was difficult due to loss of extracellular fluid. For this reason, vasodilation of working muscles was forcibly limited in order to maintain the necessary blood supply to vital organs.

The dynamics of HR, OP and CLI at this stage of the study could be interpreted as adaptation to heavier work [14], performance of which leads to a decrease in total circulating plasma [15, 16]. It is probably for this reason that we observed relative decrease in stroke volume, increase in HR and CLI toward the end of the test.

Thus, during work on the bicycle ergometer after immersion, the first group of subjects demonstrated substantial circulatory changes due to inadequate regulation of the resistive compartment of the vascular system during adaptation to immersion and decrease in adequate adaptation to moderate physical exercise.

The initial stage of exercise after immersion was characterized, in the second group of subjects, by increase in minute volume of circulation ($P<0.001$) due to increase in stroke volume ($P<0.1$), with HR dynamics similar to the background. These phenomena probably elicited more marked vasodilation ($P<0.25$) and were related to a tendency toward decrease in CU_{O_2}. Apparently, the hemodynamic changes were a compulsory measure to assure optimum delivery of O_2 to working muscles. The CLI level was indicative of low functional myocardial strain [14].

At the end of the study of this group, the initial increment of stroke volume diminished, without exceeding absolute background values; the increase in minute volume persisted with lower O_2 uptake and CU_{O_2}; the dynamics of $\dot{V}$ resembled the background. Such phenomena could appear as a result of change in correlation between oxygen capacity and blood viscosity with high Hmt, which in turn led to inadequate delivery of oxygen to working muscles as a result of decreased velocity of delivery [10].

Thus, adaptation to immersion simulating weightlessness was associated, at the early stage, with loss through the kidneys of considerable amounts of intravascular and extravascular fluid in one case and only moderate decrease in fluid in the blood stream in the other. The difference in manifestation of responses could be attributable to individual distinctions of hemodynamic regulation on the level of microcirculation, with redistribution of blood under conditions simulating some of the effects of weightlessness.

Hypohydration of the intravascular and extravascular space under immersion conditions during physical exercise was associated with circulatory changes, which could be indicative of inadequate "working" volume of circulating blood and, consequently, considerable functional strain on the cardiorespiratory system.

Tolerance of the functional load after immersion was better retained in subjects who had more endurance in performing the exercise test in the background period. Apparently, this is attributable to the capacity to mobilize the retained reserves to provide for the necessary level of circulation in the presence of changes related to impaired delivery of O_2 to working muscles.

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BLOOD COAGULATION PLASMA FACTORS AND CHANGE IN FIBRINOLYSIS DURING NEUTRAL TEMPERATURE WATER IMMERSION IN SUBJECTS WITH BORDERLINE HYPERTENSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 22 Sep 81) pp 45-48

[Article by V. N. Orlov, L. L. Kirichenko and M. A. Yunusov]

[English abstract from source] The effect of 7-day "dry" immersion on the hemocoagulation system of male test subjects, aged 45-55, was examined. The experiments were carried out on 15 volunteers, 11 of whom had boundary arterial hypertension (BAH) (according to the WHO classification) and 4 were healthy controls. The data obtained (thromboelastograms and coagulograms) show that "dry" immersion induces hypercoagulopathic changes in the hemocoagulation system. The BAH patients have displayed a more marked fibrinolysis depression, indicating a decline of their reserve-adaptive capabilities.

[Text] It is known that there is considerable loss of plasma, increase in hematocrit and blood viscosity [1, 2] during man's adaptation to weightlessness, and this could be instrumental in impairment of rheological properties of blood, as well as onset of ischemia of different organs and tissues, and thrombotic complications. It can be assumed that the substantial changes in homeostasis during simulated weightlessness could be related to age-related involution in the blood-clotting system [3] and presence of concomitant disease. According to some observations [2, 4-6], the process of change in the blood-clotting system under hypodynamic conditions is phasic. The initial increase in clotting potential of blood followed by hypocoagulation and a tendency toward bleeding when weightlessness is simulated is attributed by authors to intravascular coagulation and consumption coagulopathy. There are sparse data in the literature concerning the effect of water immersion on the blood-clotting system.

Our objective here was to investigate blood coagulation during "dry" immersion in neutral temperature water in men 45-55 years of age with borderline arterial hypertension (BAH; classification of WHO). Considering data in the literature concerning depression of the fibrinolytic blood system during immersion, it was interesting to study the change in level of blood serum α-1-antitrypsin, which is an inhibitor of the plasmin system [7].

Methods

We used the model of "dry" immersion proposed by Ye. B. Shul'zhenko and I. F. Vil'-Vil'yams [8] in our study with simulation of weightlessness. A total of 15 male volunteer subjects participated in the studies, 11 of whom had BAH and 4 healthy men made up the control group. Blood coagulation parameters (data from thromboelastography, coagulograms) and blood serum α-1-antitrypsin level were examined before immersion (background), on the 3d and 7th days of immersion, as well as in the recovery period, 48 h after termination of the test. We also determined hemocoagulation parameters at later stages of readaptation in 5 men--5 days after termination of the test. Blood was taken in the mornings, on a fasting stomach, with the subjects in supine position.

Thromboelastography and subsequent calculation of 11 parameters were performed on a Soviet GKGM-04 4-channel thromboelastograph. Plasma recalcification time (PR) was determined by the method of Bergerhot and Roka, plasma heparin tolerance (PHT) by the Pollar method, plasma fibrinogen (F) by the method of R. A. Rutberg and blood serum fibrinolytic activity (FAB) by the method of Bidkell.

We took blood from 22 healthy individuals to determine the normal values for plasma coagulation and fibrinolysis parameters. Determination of α-1-antitrypsin level was made using immunodiffusion media (plates) of the Behrinwerke Firm (FRG).

The control concentration of α-1-antitrypsin (260±31 mg%) was determined on the basis of 25 blood serum tests on healthy individuals. The obtained data were submitted to processing by the method of variation statistics.

Results and Discussion

Comparative analysis of hemocoagulation parameters of plasma revealed that the thromboelastograms (TEG) and coagulograms (CG) of subjects with BAH (main group) did not differ appreciably from those of the control group in the background period (Tables 1 and 2). The level of α-1-antitrypsin in the main and control groups also failed to exceed the norm established for healthy individuals (260± 31 mg%). We see from Table 2 that, on the 3d day of "dry" immersion there were marked changes in the blood-clotting system in the main group of subjects. We demonstrated a significant reduction of reaction time (R) and fibrinolytic activity (FA) of blood, as compared to the background period ($P<0.001$). There was a tendency toward increase in maximum clotting time (t) and clot elasticity (E). The other TEG parameters--clotting rate (K), maximum amplitude (ma), total clotting time (T), syneresis (Si) and its constant (S), clot retraction (CR) and angle α--did not change appreciably. Maximum dynamics of TEG parameters were observed on the 7th day of immersion: there was even greater reduction of reaction time, Si decreased almost to one-half, blood T and angle had a tendency toward reduction. CG parameters showed statistically reliable increase in F and significant decline of FAB. There was a tendency toward PHT decrease.

Comparative analysis of data referable to blood coagulation and anticoagulation systems in both groups of subjects (see Tables 1 and 2) reveals that changes in most coagulation parameters, although there were differences between groups, presented essentially the same direction, in the form of increase in hypercoagulopathic potential of blood, which should be evaluated as a manifestation of the

adaptation syndrome in response to altered gravity. In the subjects with BAH, the changes in some TEG (R, FA) and CG (F, FAB) parameters were more significant already on the 3d day of immersion, as compared to the group of healthy subjects. This was particularly evident in the considerable depression of FAB. The tendency toward depression of fibrinolysis in the main group also continued in the early recovery period (48 h after immersion), whereas in the control group the parameters of fibrinolysis reverted to the base level by this time. Further observation revealed that normalization of FAB occurred on the 5th day of the readaptation period in the main group of subjects.

Table 1. Hemostasis plasma factors and α-1-antitrypsin level in control group of subjects submitted to "dry" immersion

PARAMETER OF PLASMA HEMOSTASIS	NORMAL	BEFORE IMMERSION (BACK-GROUND)	DAY OF IMMERSION		RECOVERY PERIOD
			3	7	
		TEC			
R, MIN	5,02±0,25	5,0±,023	3,84±0,15	2,72±0,14*	5,0±0,23
K, MIN	3,1±0,49	2,45±0,21	2,41±0,20	2,10±0,23	2,49±0,28
ma, UNITS	53,5±2,30	53,2±2,12	55,5±1,73	57,9±0,98	53,3±2,10
E, %	134,0±11,12	131,40±7,34	138,8±8,01	145,0±6,23	134,8±10,3
t, MIN	13,72±0,71	13,50±0,64	13,0±0,24	12,36±0,24	13,55±0,37
S, MIN	16,92±1,13	16,82±1,03	15,2±0,92	14,7±0,94	16,90±1,02
T, MIN	22,25±1,62	21,74±1,60	21,5±0,92	17,24±1,12	21,9±1,05
SI, UNITS	7,44±0,70	7,50±0,55	6,80±0,47	4,34±0,21**	7,42±0,22
ANGLE α, DEGREES	13,51±1,08	13,50±0,90	15,62±0,77	5,12±1,12**	13.47±0,83
CR, %	5,73±0,42	5,1±0,32	4,8±0,22	5,12±0,34	5,5±0,30
FA, %	19,74±0,39	19,82±0,80	15,10±0,70**	11,52±0,98*	19,1±0,98
		CG			
F, MG%	309,91±31,20	300,0±10,42	327,4±10,50	365,14±10,3***	310,5±15,4
FAB, %	20,11±0,41	20,20±1,37	14,48±0,90	10,92±0,80*	21,15±0,92
PR, MIN	1,81±0,13	1,73±0,16	2,0±0,13	1,30±0,10	1,75±0,12
PHT, MIN	8,50±0,80	9,24±0,34	10,45±0,42	6,41±0,31**	9,10±0,72
α-1-ANTITRYPSIN, MG%	260±31	250,0±26	220,0±20	220±26	230±34

Here and in Table 2: *P< 0.001 **P<0.01 ***P<0.02

Our data may be indicative of presence of hypercoagulopathic tendencies in the blood-clotting system during "dry" immersion, as well as inertia of adaptation mechanisms of the "fibrinolytic element" of this system in individuals with BAH. The increase in clotting properties of blood under conditions simulating weightlessness is, in the opinion of a number of authors [1, 2, 4, 9], attributable to a decrease in blood flow velocity, impairment of vascular permeability and discharge of coagulants from formed blood elements.

It is apparent from the submitted material that the level of α-1-antitrypsin had a tendency toward decline with increase in exposure to immersion conditions. This tendency was less pronounced in the control studies. In view of the fact that α-1-antitrypsin is a blocking agent for the plasmin system [7], the decline of its level concurrently with depression of fibrinolysis is apparently due to the body's defense reaction aimed at eliminating the plasmin system block and improving blood consistency [flow].

Table 2. Plasma hemostasis and α-1-antitrypsin level in subjects with BAH submitted to "dry" immersion

PARAMETER OF PLASMA HEMOSTASIS	NORMAL	BEFORE IMMERSION (BACK-GROUND)	DAY OF IMMERSION		RECOVERY PERIOD(DAY)	
			3	7	2	5
			TEG			
R, MIN	5,02±0,25	4,88±0,22	3,35±0,16*	2,53±0,43*	4,23±0,20	5,0±0,24
K, MIN	3,1±0,49	2,42±0,21	2,42±0,21	2,12±0,17	2,53±0,22	2,54±0,22
ma, UNITS	53,5±2,3	53,0±2,10	55,4±1,98	57,8±1,97	54,51±1,95	53,7±2,11
E, %	134,0±11,12	130,01±8,05	139,8±7,81	144,2±7,12	139,3±8,34	135,81±9,4
L, MIN	13,72±0,71	13,35±0,52	16,12±0,44	12,2±0,52	12,55±0,50	14,03±0,73
S, MIN	16,92±1,13	16,73±1,04*	17,1±0,93	13,7±0,95	14,82±1,41	16,5±1,10
T, MIN	22,25±1,62	19,37±1,02	20,72±1,04	17,11±1,01	18,42±0,98	22,04±1,52
S_I, UNITS	7,44±0,70	7,9±0,58	6,88±0,57	4,16±0,4*	8,1±0,73	7,9±0,62
ANGLE α, DEGREES	13,51±1,08	13,2±0,92	15,17±0,98	19,32±1,1*	15,20±0,87	13,0±0,89
CR, %	5,73±0,42	5,4±0,20	4,46±0,28	6,96±0,44**	5,85±0,22	5,72±0,23
FA, %	19,74±0,39	20,01±0,40	14,67±0,17*	10,38±0,22*	12,33±0,32*	19,55±0,28
			CG			
F, MG%	309,91±31,20	295,97±10,51	336,18±11,04	362,50±12,31*	324,12±12,01	311,10±9,2
FAB, %	20,11±0,41	19,92±0,38	14,52±0,23*	11,08±0,18*	15,02±0,51*	19,84±0,36
PR, MIN	1,81±0,13	1,68±0,14	2,02±0,15	1,39±0,11	1,73±0,12	1,74±0,14
PHT, MIN	8,5±0,80	10,44±0,42	10,47±0,43	6,39±0,24*	8,71±0,34**	8,52±0,33*
α-1-ANTITRYPSIN, MG%	260±31	205±50	275±25	176±24	176±19	—

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HUMAN HEMODYNAMIC PARAMETERS DURING EXPOSURE TO CONTINUOUSLY INCREASING ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 4 Feb 82) pp 48-52

[Article by D. Yu. Arkhangel'skiy and L. S. Plakhotnyuk]

[English abstract from source] The effect of acceleration on central hemodynamics was investigated in centrifugation experiments. Also examined was the protective effect of muscle tension, anti-G suit, and of an altered acceleration vector. It was demonstrated that visual disorders were caused by a decrease in cardiac output. The countermeasures diminished the rate with which cardiac output declined due to the higher values of stroke volume that were produced by the anti-G suit and a changed body position. Arbitrary muscle tension ensured the effect only as a result of increased heart rate.

[Text] Displacement of blood from the upper part of the body to vessels of the abdominal cavity and legs is one of the main hemodynamic effects on man of head-pelvis accelerations. As a result of this, there is decreased venous return of blood to the heart, systolic pressure in the basin of the carotid artery drops, which leads to onset of visual disorders [1, 2].

The means of protection against the effects of accelerations in current use prevent deposition of blood in vessels of the lower part of the body, cause relative increase in venous return and, consequently, widen the range of endurance of accelerations. However, the question of change in hemodynamic parameters during exposure to accelerations with and without use of protective measures has not been sufficiently investigated.

Our objective here was to determine the changes in some hemodynamic parameters under the effect of continuously increasing accelerations with use of various protective measures.

Methods

We conducted 2 series of tests with accelerations that were increased at the rate of 0.1 G/s to the limit of endurance using a centrifuge with the participation of 7 male subjects 19-23 years of age, with and without use of protective

measures--G-suit of the chamber type and voluntary muscle tension. The range of endurance was determined according to loss of peripheral vision (increase in latency period of motor reaction to photic stimulus ⩾2 s). In the first series of tests, the subjects were at a 30° angle to the acceleration vector and in the second, at a 55° angle.

We recorded continuously before, during and in the 1st-5th min of the aftereffect period the electrocardiogram in the three Neba leads (EKG), heart rate (HR), systolic blood pressure (BP) in arteries of the earlobe and tetrapolar rheogram of the chest. We used the Kubicek formula [3] to determine cardiac stroke volume (SV) and calculated minute blood volume (MV).

The obtained data were submitted to statistical processing.

Results and Discussion

With the muscles relaxed and the subject at a 30° angle to the vector of acceleration, the limit of endurance constituted 5.11±0.05 G without the GS [G-suit] and 7.3±0.11 G wearing the GS, and during voluntary muscular tension without the GS it was 8.8±0.21 G [units].

As a result of our studies, we demonstrated a distinct difference in change of parameters of central hemodynamics depending on the experimental conditions (Table 1).

According to the data listed in Table 1, the chronotropic reaction of the heart was determined by the limit of endurance, and it ranged from +66% with muscle relaxation without the GS to +118% with voluntary muscle tension. With the muscles relaxed SV decreased by about 50%. With deliberate tension of muscles, VC decline was more marked, whereas MV did not change due to higher HR than during relaxation. In general, MV diminished to a lesser extent than SV; however, with increase in accelerations BP inevitably dropped to 40-50 mm Hg in the earlobe vessels, i.e., to levels inherent in onset of visual disturbances.

All of the hemodynamic parameters studied showed changes that were linear to the increase in accelerations, with a reliable correlation between acceleration levels and recorded parameters (Figure 1). The equations of regression corresponding to Figure 1a in relaxed position were: $HR_r = 76+6 \cdot n_{cf}$ with coefficient of correlation $r = +0.632$, $P<0.001$, and with tensed muscles $HR = 87+9 \cdot n_{cf}$, $r = 0.954$, $P<0.001$.* With the GS, HR increased more slowly: $HR = 77 + 5 \cdot n_{cf}$, $r = +0.849$, $P<0.001$. Cardiac output dropped the most sharply during relaxation without the GS: $SV = 80.2 - 8.3 \cdot n_{cf}$, $r = -0.895$, $P<0.001$. The rate of decline of SV was the same with use of protective measures: $SV = 66.0 - 5.3 \cdot n_{cf}$, $r = -910$, $P<0.001$ with voluntary muscle tension and $SV = 70.5 - 5.1 \cdot n_{cf}$, $r = -0.890$, $P<0.001$ in the experiments with GS (see Figure 1b). Without protective measures, MV diminished in accordance with the equation, $MV = 6.35 - 0.49 \cdot n_{cf}$, $r = -0.792$, $P<0.001$ during relaxation, whereas with tensed muscles or in the GS the rate of decline per unit acceleration was lower by about half: $MV = 6.17 - 0.24 \cdot n_{cf}$, $r = -0.880$, $P<0.001$ with tense muscles and $MV = 6.12 - 0.27 \cdot n_{cf}$, $r = -0.840$, $P<0.001$ in the GS.

*Translator's note: Subscript cf ("tsf") probably refers to centrifuge.

Table 1. Hemodynamic changes during exposure to continuously increasing accelerations at 30° angle

PARAMETER	EXPERIMENTAL CONDITIONS	BACK-GROUND	ACCELERATIONS, G							
			1	2	3	4	5	6	7	8
HR/MIN	NO GS, RELAXATION	70±3	86±4	97±3	102±4	109±4	116±4			
	GS, RELAXATION	70±5	84±6	96±6	101±5	99±6	106±6	114±6	124±8	
	NO GS, TENSION	76±6	98±4	109±5	116±2	125±1	135±1	145±2	154±3	160±3
BP, MM HG	NO GS, RELAXATION	84±2	84±4		71±6		35±6		—	
	GS, RELAXATION	78±5	70±7		64±6		56±7		48±7	
	NO GS, TENSION	80±3	80±4		72±7		62±6		58±4	
SV, %	NO GS, RELAXATION	100	—16	—27	—38	—46	—53	—	—	—
	GS, RELAXATION	100	—12	—21	—27	—34	—43	—48	—52	—
	NO GS, TENSION	100	—23	—31	—40	—46	—53	—58	—64	—67
MV, %	NO GS, RELAXATION	100	—7	—13	—21	—29	—37	—	—	—
	GS, RELAXATION	100	+1	—2	—9	—17	—20	—22	—28	—
	NO GS, TENSION	100	+2	—2	—6	—10	—14	—19	—26	—30

Table 2. Hemodynamic changes during exposure to accelerations at 55° angle to long axis of body

PARAMETER	EXPERIMENTAL CONDITIONS	BACK-GROUND	ACCELERATIONS, G									
			1	2	3	4	5	6	7	8	9	10
HR/MIN	NO GS, RELAXATION	72±6	79±5	88±5	90±4	96±4	100±3	103±3	104±4	105±4	—	—
	GS, RELAXATION	74±5	80±5	88±6	89±7	93±7	96±8	97±8	96±9	97±12	95±20	
	NO GS, TENSION	84±6	97±6	102±5	109±5	114±5	122±7	129±7	134±6	139±6	142±6	146±5
BP, MM HG	NO GS, RELAXATION	93±6	93±6		87±3		82±4		78±4		—	
	GS, RELAXATION	90±6	87±9		87±9		90±10		90±10		—	
	NO GS, TENSION	98±4	102±2		100±4		95±3		90±7		87±8	
SV, Δ %	NO GS, RELAXATION	100	—14	—26	—31	—37	—44	—49	—51	—57	—	—
	GS, RELAXATION	100	—12	—23	—29	—32	—37	—44	—51	—54	—57	—
	NO GS, TENSION	100	—19	—24	—32	—37	—42	—50	—55	—61	—66	—69
MV, Δ %	NO GS, RELAXATION	100	—9	—9	—12	—16	—21	—27	—30	—36	—	—
	GS, RELAXATION	100	+3	—5	—10	—16	—20	—27	—33	—37	—38	—
	NO GS, TENSION	100	—3	—6	—7	—9	—13	—20	—27	—33	—38	—41

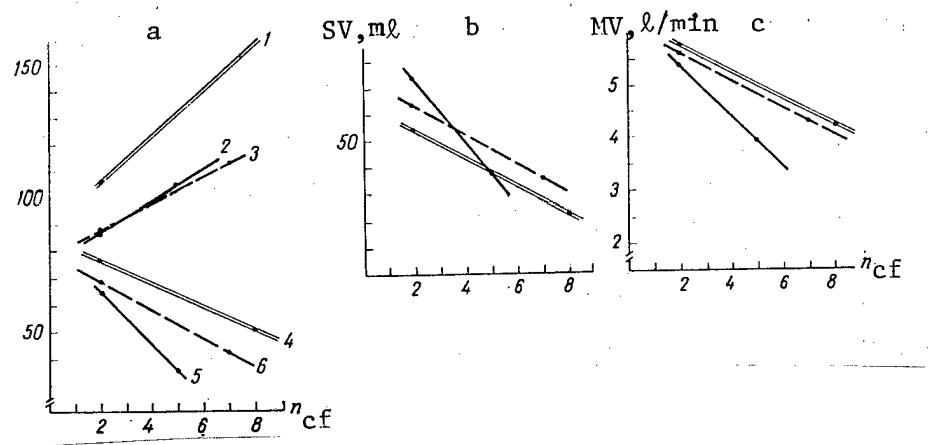

Figure 1. Lines of regression of parameters HR and BP (a), SV (b) and MV (c) during exposure to accelerations at 30° angle

Here and in Figure 2:

1-3) HR (per min) thin line: no GS and relaxation dash line: in GS and relaxation

4-6) BP (mm Hg) boldface: no GS and tension

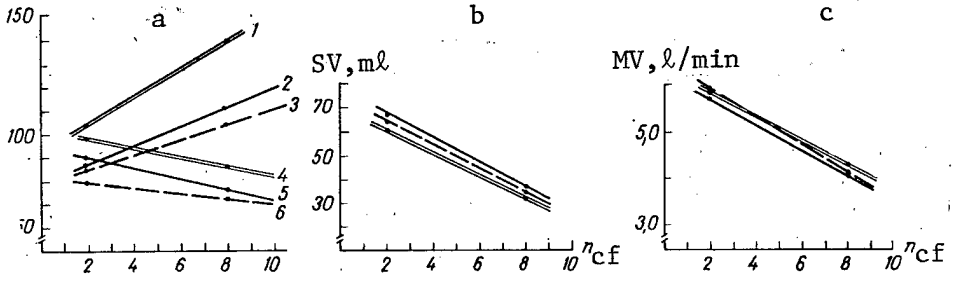

Figure 2. Lines of regression of parameters HR and BP (a), SV (b) and MV (c) with exposure to accelerations at 55° angle

Thus, the results of the first series of tests revealed that protective measures improved endurance of continuously increasing accelerations due to retention of MV, which maintains higher BP on the eye level. However, with tense muscles, this is determined by higher HR, whereas with use of GS by less decline of SV.

In the second series of tests, endurance increased by an average of 2 G, constituting in relaxed position 8.06±0.2 G without the GS, 8.67±0.12 G in the GS and 10.78±0.22 S with voluntary muscle tension and without the GS.

Accelerations elicited a +28% increase in HR in the tests with GS and +75% without GS with tensed muscles, which is considerably lower than the HR increment observed in the first series of studies.

In the tests conducted with subjects in relaxed position, SV smoothly declined with increase in accelerations and constituted about 40% of the base value at

the time maximum endurance was reached. With voluntary muscle tension, SV diminished more slowly, but to lower values.

As accelerations increased MV decreased by an average of 40% by the time maximum endurance was reached, and it declined at a slower rate with voluntary muscular tension due to greater increment of HR than when relaxed. In spite of the fact that SV and MV diminished just as they did in the first series of studies with the subject at an angle of 55° to the vector of acceleration, BP in earlobe vessels dropped insignificantly (by about 10%; Table 2) at the time peripheral vision was lost, and it was higher than with exposure to accelerations at an angle of 30°.

Statistical processing of data obtained in the second series of tests enabled us to demonstrate a correlation between the parameters studied and magnitude of accelerations (Figure 2). The lines of regression illustrated in Figure 2 corresponded to the following equations for changes in HR: $HR = 78+4 \cdot n_{cf}$ with the subjects relaxed without the GS, $HR = +79+3 \cdot n_{cf}$ wearing the GS ($r = +0.693$ and $+0.753$, $P<0.001$). During voluntary muscular tension, HR increased faster: $HR = 91+6 \cdot n_{cf}$, $r = +0.861$, $P<0.001$.

Regardless of the measure used for protection against accelerations, SV decreased by an average of 5 mℓ/G: $SV = 74.8-5.1 \cdot n_{cf}$ with relaxed muscles and no GS and $SV = 74.8-4.9 \cdot n_{cf}$ with the GS. During voluntary tension of muscles, SV decreased in accordance with the following formula: $SV = 68.9-4.6 \cdot n_{cf}$, $r = -0.93$, -0.780 and -0.900, respectively, $P<0.001$.

The rate of decline of MV was about the same: $MV = 6.22-0.27 \cdot n_{cf}$ in relaxed position without GS and $MV = 6.48-0.29 \cdot n_{cf}$ with the GS. During voluntary tension of muscles, this parameter decreased in accordance with the following formula: $MV = 6.38-0.26 \cdot n_{cf}$, $r = -0.78$, -0.89 and -0.930, respectively, $P<0.001$.

Thus, in the course of the tests we demonstrated distinct differences in the hemodynamic parameters studied under the effect of continuously increasing accelerations, depending on use of protective measures and the subject's position.

Upon reaching the limit of endurance in relaxed position, with exposure to accelerations at an angle of 30°, the most typical changes were decline of SV and MV, with corresponding drop of systolic BP at eye level. A drop of BP to 40-50 mm Hg was observed when MV decreased by about 40% in comparison to the base level (3.8-4.2 $\ell \cdot m^{-1}$ in absolute figures).

Use of measures for protection against accelerations--voluntary tension of leg and abdominal muscles, wearing GS or altering direction of vector of acceleration--retarded the rate of decline of MV, which resulted in increasing the limit of endurance of accelerations. However, while the GS and altered position maintained MV primarily due to higher SV levels, voluntary muscular tension did so exclusively by means of high HR values.

Analysis of changes in MV with consideration of the component of acceleration on the y axis yielded the following equation of regression: $MV = 6.40-0.55 \cdot n_y$ (in liters/min) with relaxed muscles ($r = -0.826$, $P<0.001$). According to this

formula, we should expect development of visual disturbances upon reaching accelerations on the order of 4 G, which is consistent with the data of a number of authors [4-6].

Our findings here demonstrated the informativeness of tetrapolar rheography for assessing acute hemodynamic changes [7] with exposure to peak-like accelerations, as well as the possibility of using this method to assess the efficacy and physiological cost of various anti-G protective measures.

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RAT REACTIONS TO IMMOBILIZATION STRESS FOLLOWING SPACEFLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 25 Jan 81) pp 52-57

[Article by L. V. Serova]

[English abstract from source] The study of male Wistar rats flown on the biosatellite Cosmos-1129 showed that 7-10 hours after recovery they developed a distinct stress-reaction of blood cell elements (increased neutrophil and decreased lymphocyte counts) and the thymus (decreased thymocyte count). Despite this, the level of their reaction (as a percentage of the preflight values) to additional immobilization stresses was similar to that of controls. As a result, by the end of immobilization tests deviations from the physiological norm in the flown animals were greater and their reserve capabilities were lower than in the controls.

[Text] Experiments with mammals (Wistar rats] flown aboard biosatellites of the Cosmos series led to the conclusion that rather prolonged weightlessness (18-22 days, i.e., about 1/50th of their life expectancy) does not elicit pathological structural and functional changes in any of the internal organs. The changes demonstrated postflight in the hypothalamo-hypophyseo-adrenal system, muscles, bone, myocardium and other organs were reversible. They were virtually absent when animals were examined 25 days after returning to earth [1-4].

At the same time, it must be noted that in the studies pursued heretofore, the animals were in a state of relative rest. Moreover, it was found that general amount of activity was smaller in animals exposed to weightlessness than in the control for the first few days after returning to earth. There is reason to believe that this adaptive reaction of the body--physiological restriction of mobility--was instrumental in maintaining homeostasis and retaining physiological norms in the recovery period with regard to most organs and functional systems. Constitutional resistance was diminished, already after an 18-22-day spaceflight, and although the decline was insignificant, the appearance in flight or the readaptation period of some load situations could lead to appreciable decrease in the body's reserve capabilities [5, 6]. For this reason, the purpose of the experiment described here, which was conducted aboard Cosmos-1129 biosatellite, was to assess the reactions of animals returned to earth after a spaceflight to a series of immobilization stress tets performed in the recovery period. The reactions were evaluated on the basis of cytology of peripheral blood and the thymus.

Methods

In our experiments, we used male Wistar rats from the vivarium of the Institute of Experimental Endocrinology (Bratislava, CSSR). When we started, the age of the animals was 84-86 days and they weighed 290 g.

During the spaceflight, which lasted 18.5 days, the animals were kept separately in box-cages. The cages were 26 cm in length and 9.5 cm in diameter [7]. Air temperature in the region of the cages was in the range of 23.5-25.5°C, relative humidity 55-65%, pO_2 135-212 mm Hg, pCO_2 up to 6 mm Hg. Inflight daylight lasted 12 h.

Concurrently with the flight, we conducted a ground-based synchronous control experiment in a mock-up of the biosatellite, where we simulated the conditions of onboard animals, microclimate parameters, as well as physiologically relevant factors (vibration, accelerations, impact accelerations) related to launching and landing the biosatellite [8]. The rats in the vivarium control group were kept in separate cages 20×35×54 cm in size at air temperature of 22-25°C during the experiment.

All groups of animals (flight, synchronous and vivarium controls) were given paste-form special feed [9], in amounts of 40 g/day/rat and water.

The animals in the first experimental group (7 rats) were decapitated 7-10 h after the flight, those in the second group (6 rats) were decapitated 6 days after the flight. Before this, they were kept in separate cages 18×18×12.5 in size and continued to receive special feed, increasing the daily allowance to 45 g/rat. The third group of animals (7 rats) were kept under the same conditions as the second group after the flight, but submitted to functional tests: on the day of landing (0 day) and on the 3d, 4th, 5th and 6th days of the readaptation period. As the functional test, we used immobilization stress (for 2.5 h) with the animals in prone position [10]. During the tests performed on 0, 3d and 5th days we collected blood from the animals (from an incision in the tail) before immobilization, at the end of the test and 30 min after it was terminated. The animals were decapitated after the last test on the 6th day of the recovery period.

We examined rats in the vivarium and synchronous control groups following an analogous program.

We analyzed the leukocyte formula of peripheral blood in smears stained according to Romanovskiy-Giemsa. The thymus was weighed, part of the organ was fixed in 3% acetic acid, homogenized, then we counted thymocytes; the other part of the organ was fixed in Carnoy fluid and imbedded in paraffin; sections were stained with hematoxylin and eosin.

The digital material was processed using Student's t criterion.

Results and Discussion

In animals examined 7 h after the spaceflight, before the functional tests, we already observed the typical changes associated with the stress reaction:

decreased lymphocyte count and increased segmented neutrophil count. Total concentration of leukocytes presented a tendency toward increase. However, the differences in parameters, as compared to the control, were unreliable. The lymphocyte/neutrophil ratio was decreased to more less than 1/3 of the parameters in the vivarium control (Tables 1 and 2). All these blood changes were analogous to those observed after other flights [11], and they represent an acute reaction to landing, the main stress factor apparently being the return to earth's gravity. This reaction was virtually absent in the synchronous control experiment (see Tables 1 and 2); we merely observed some decline in lymphocyte count, whereas neutrophils and lymphocyte/neutrophil ratio remained unchanged. The fact that this reaction was observed only in the first few post-flight hours and, with immobilization stress tests, only on the day of the test confirms that it develops acutely at the final stage of the flight. Subsequently, normalization occurs. The parameters obtained in blood tests on the 3d and 5th days after landing, before the stress tests, did not differ in flight group animals from those of both animals submitted to stress and intact vivarium experiment (see Tables 1 and 2).

Table 1. Blood leukocytes on 0, 3d and 5th days after flight in Cosmos-1129 biosatellite (before stress tests; n = 7).

POST-FLIGHT DAY	ANIMAL GROUP	LEUKOCYTES, THOU/MM^3	LYMPHOCYTES, THOU/MM^3	SEGMENTED NEUTROPHILS, THOU/MM^3
	VIVARIUM CONTROL (B)	8,2±0,5	5,18±0,51	2,4±0,3
0	SYNCHRONOUS EXPERIMENT(C)	6,6±0,7	4,03±0,35	2,3±0,3
	FLIGHT	9,5±1,5	3,24±0,40 $P_B<0,02$	6,1±1,4 $P_{B,C}<0,05$
	VIVARIUM CONTROL	8,4±0,7	5,69±1,13	2,50±0,20
3	SYNCHRONOUS EXPERIMENT	9,0±0,8	4,92±0,49	3,31±0,67
	FLIGHT	8,7±1,0	5,34±0,43	3,01±0,81
	VIVARIUM CONTROL	8,2±0,9	5,29±0,56	2,47±0,55
5	SYNCHRONOUS EXPERIMENT	11,4±0,9 $P_B<0,05$	7,29±0,84	3,58±0,31
	FLIGHT	6,5±0,7 $P_C<0,001$	4,19±0,36 $P_C<0,01$	2,10±,040 $P_C<0,02$

In spite of the severely marked stress reaction of cellular elements of blood, which was demonstrated when experimental animals were examined 7 h after the flight, performance of an additional immobilization stress test (2.5 h) against this background was associated with the same reaction in the experiment and control: general leukocytosis, further increase in neutrophil count and decrease in lymphocyte count.

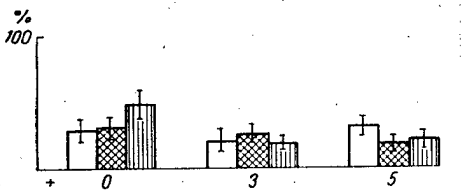
The severity of the reaction that developed in response to the stress test was virtually the same in the experiment and control. Thus, the lymphocyte/neutrophil ratio after the stress test on 0 day constituted 33% of the base (before the test) value, 24% in the synchronous experiment and 22% in the vivarium control. However, the difference in severity of reaction was unreliable (see Figure). Since this ratio was already considerably lower in the experimental group even before the stress test than in controls (see Table 2), it was lower at the end of the test (0.21, versus 0.51 in the vivarium and 0.44 in the synchronous control) and 30 min later (0.11, versus 0.24 and 0.22 in the control groups).

Table 2. Lymphocyte/neutrophil ratio in blood of animals during stress tests performed after flight aboard Cosmos-1129 biosatellite

ANIMAL GROUP	POSTFLIGHT DAYS								
	0			3			5		
	BEFORE TEST	AT END OF TEST	AFTER TEST	BEFORE TEST	AT END OF TEST	AFTER TEST	BEFORE TEST	AT END OF TEST	AFTER TEST
VIVARIUM CONTROL (B)	2,37±0,36	0,51±0,08	0,24±0,02	2,39±0,34	0,35±0,05	2,3±0,55	2,73±0,56	0,67±0,16	0,77±0,26
SYNCHRONOUS EXPERIM (C)	1,83±0,15	0,44±0,07	0,2±0,03	2,06±0,36	0,37±0,05	0,24±0,04 $P_B<0,01$	2,08±0,25	0,27±0,02 $P_B<0,05$	0,43±0,12
FLIGHT	0,64±0,13 $P_{B,C}<0,001$	0,21±0,02 $P_{B,C}<0,01$	0,11±0,02 $P_B<0,001$ $P_C<0,01$	2,55±0,66	0,30±0,03	0,17±0,03 $P_B<0,002$	2,40±0,40	0,57±0,15	0,37±0,05

Table 3. Weight of thymus (mg) and thymocyte count (TC--millions) after experiment aboard Cosmos-1129

ANIMAL GROUP	7-10 H AFTER LANDING			6TH DAY OF READAPTATION TO EARTH					
	WITHOUT ADDITIONAL FACTORS						WITH ADDITIONAL STRESS TESTS		
	MASS, MG	TC MILLION/ 100 MG	TC MILLION/ ORGAN	MASS, MG	TC MILLION/ 100 MG	TC MILLION/ ORGAN	MASS, MG	TC MILLION/ 100 MG	TC MILLION/ ORGAN
VIVARIUM (B)	394±26	280±30	1126±173	186±26	279±30	797±70	200±14	249±28	497±55
SYNCHRON. (C)	309±13 $P_B<0,02$	279±21	866±78	337±26	317±20	1079±125 0,05	152±19 0,05	288±14	437±54
FLIGHT	252±14 $P_B<0,001$ $P_C<0,02$	280±16	704±47 $P_B<0,05$	206±10 $P_B<0,02$ $P_C<0,001$	274±15	564±31 $P_B<0,01$ $P_C<0.002$	128±8 $P_B<0,001$	260±13	331±34 $P_B<0,05$



Lymphocyte/neutrophil ratio in peripheral blood. Severity of reaction (% of base level) at end of stress test, 0, 3d and 5th postflight days
White columns--vivarium control animals; crosshatched--synchronous experiment; striped--animals flown in biosatellite

Prior to the stress tests performed on the 3d and 5th days of the recovery period, the leukocyte formula was the same in the flight group as in control animals. The lymphocyte/neutrophil ratio constituted 2.40-2.55, versus 2.06-2.73 in control groups (see Table 2). There was also the same degree of changes developing in response to immobilization (see Figure). Accordingly, there was no reliable difference in absolute values of this parameter at the end of the test in experimental and control animals. There was considerably faster recovery after the stress test on the 3d day of the readaptation period in vivarium control animals than in the flight and synchronous experiment groups. An analogous tendency, but less marked was observed also on the 5th day of the readaptation period (see Table 2).

In animals decapitated 7-10 h after the flight, we found a decrease in weight of the thymus and total thymocyte content in this organ (Table 3), which conforms to previous findings [12-14]; thymocyte content per 100 mg tissue did not change. There was also a decrease in thymus mass in animals of the synchronous experiment, but less marked than in the flight group of rats.

Histological examination of the thymus at this time revealed findings analogous to those described previously [13, 14]; there was enlargement of pyknotic nuclei and nuclear detritus. However, it should be noted that these changes were less marked than in the preceding experiments: pyknosis constituted 1-3/field of vision (at 900× magnification) and was massive in only 1 out of 7 cases. The quantity of pyknoses did not show a correlation with extent of loss of organ weight. This warrants the assumption that loss of thymocytes at this time occurred mainly due to migration from the organ and, to a lesser extent, due to disintegration. This was indicated by the absence of signs of phagocytosis and increase in number of Hassall's corpuscles.

There was further decrease in weight of the thymus and total thymocyte count by the 6th postflight day in the experimental group of animals (see Table 3), whereas cellularity and weight of this organ were restored to normal values in the synchronous control. It should be noted that, at this time, we observed a decrease in thymus weight and in quantity of thymocytes in vivarium control animals (as compared to the animals in the control group decapitated on 0 day), which could be related to moving the animals from usual vivarium cages to metabolic ones. Nevertheless, the difference in organ weight and total number of thymocytes in flight and control groups of animals was reliable and, as at the first examination, there was no change in number of thymocytes per 100 mg tissue (see Table 3).

The set of immobilization stress tests performed on 0, 3d, 4th, 5th and 6th postflight days elicited a similar reaction in all groups of animals: decrease

in thymus mass and total number of thymocytes (see Table 3). And, in spite of the distinct involution of the thymus noted in experimental animals immediately after the flight, their reaction to additional stress was quantitatively the same as in the vivarium control: 38 and 30%, respectively, for weight; 41 and 38% for number of thymocytes. Obviously, the weight and "cellularity" of the thymus of experimental animals were lower in experimental animals after the test than in the control (see Table 3). Histological examination of the thymus of animals submitted to a set of stress tests revealed considerable increase in number of pyknotic nuclei and nuclear detritus in all groups of animals (maximum pyknosis in the flight group of animals and minimal in the vivarium control). We observed increase in layers of connective tissue, number of reticular cells and Hassall corpuscles in animals of all groups submitted to additional stress. All of these changes were considerably more marked in the flight experiment than in controls: trabeculae of connective tissue occupied large areas, there was considerable increase not only in number but size of Hassall's corpuscles; pyknotic nuclei in some of the zones formed entire accumulations; the boundary between cortical and medullary substances ceased to be distinct.

Thus, in spite of the presence of a stress reaction by cellular elements of blood (neutrophilia, lymphopenia) and thymus (decrease in thymocyte count), which was demonstrated in the flight group of animals 7-10 h after returning to earth, the severity of these reactions to subsequent immobilization stress tests (as percentage of base level) was found to be the same as in control groups of animals.

Since neutrophilia, lymphopenia and involution of the thymus under stress occur in response to more intensive release of corticosteroids, it is interesting to note that Kvetnansky et al. [15] made analogous findings in assaying corticosterone concentration in blood plasma and adrenals of the same animals as we examined. In the flight group of animals, 7-10 h after landing, they found more than 3-fold increase in corticosterone concentration in plasma and almost 2-fold increase in the adrenals, as compared to vivarium control animals. By the 6th day of the recovery period, there was a tendency toward normalization of corticosterone level, although it remained higher than in the control. The severity of the reaction to a series of immobilization stress tests (as compared to animals examined at the same time but not submitted to stress) was the same in flight and control rats, but absolute concentration of corticosterone in plasma of stressed animals in the flight group was reliably higher than in the analogous vivarium control group.

As we know, the principal purpose of the stress reaction is to mobilize the body's energy and structural resources, addressed to systems that function more intensively; for this reason, the fact that animals who returned from the spaceflight retained the capacity to react to additional stress tests could apparently be interpreted as positive. At the same time, the reaction of experimental animals to immobilization stress was quantitatively the same as in control animals. It developed against the background of analogous changes, which had already occurred by the time of return to earth, and were virtually summated with them. As a result, toward the end of the immobilization tests, the deviation of the parameters studied from the physiological norm was considerably greater in experimental animals than controls, and reserve capabilities of the organism were lower.

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ACTIVITY OF GLYCOGENOLYTIC ENZYMES IN RAT BONES AFTER FLIGHT ABOARD COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 2 Apr 82) pp 57-60

[Article by I. A. Popova]

[English abstract from source] In order to study the effect of weightlessness on metabolic processes in the bone organic matrix, α-amylase and aldolase activities in the ulnar bone of rats flown on Cosmos-1129 were measured. The activity of α-amylase and especially of aldolase was increased 6-10 hours after flight. The enzymic changes were the greatest in the animals exposed to weightlessness. The postflight exposure of the rats of the three experimental groups to immobilization produced different changes in the activity of the glycogen-splitting enzymes: it was either stimulated or inhibited. The findings suggest that the enzymes involved in glycogen splitting in the bone organic matrix of rats flown for 18.5 days probably aim at eliminating the adverse effects of weightlessness.

[Text] An experiment conducted aboard Cosmos-936 biosatellite revealed that there was appreciable activation of acid phosphatase under the effect of the spaceflight in rat antebrachial bones, which was associated with decrease in alkaline phosphatase activity [1]. Since these enzymes are involved in processes of bone resorption (acid phosphatase) and formation (alkaline phosphatase), the loss of bone tissue mass, which has been observed in man and animals during spaceflights [2, 3], could occur as a result of both increase in amount of minerals released from bones and decrease in access of mineral substance to the bone matrix.

Changes in the organic bone matrix could be a possible cause of diminished mineralization of bone. Glycogen is one of the important constituents of the bone matrix. There are data [4] to the effect that, at the time of highest mineralization of bone, there is a decrease in its glycogen content, while activity of glycogenolytic enzymes remains high.

Degradation of glycogen in bone tissue is effected primarily by hydrolysis with participation of α-amylase (EC 3.2.1.1). With regard to other enzymes of glycogenolysis in bones, aldolase (fructose-1,6-diphosphate glyceraldehyde-3-phosphate-lyase--EC 4.1.2.13) has high activity.

In order to investigate the effect of weightlessness on metabolic processes in the bone matrix, we assayed in this study the activity of α-amylase and aldolase in the ulnar bone of rats flown in Cosmos-1129 biosatellite.

Methods

These studies were conducted on male Wistar SPF rats (Bratislava, CSSR), which were flown for 18.5 days in space aboard Cosmos-1129 biosatellite. Experimental conditions were described previously.

We removed thoroughly all soft tissues from the ulnar bone, froze it in liquid nitrogen and stored it at a temperature of -50°C until it was processed. Amylase and aldolase activity was determined in the supernatant fluid after centrifuging homogenized bone for 20 min at 4000 r/min. We used a sensitive colorimetric method for quantitative assay of α-amylase, with the standard kits of the Pharmacia Firm (Sweden) to determine activity of this enzyme. Aldolase activity was measured by the spectrophotometry method according to rate of conversion of fructose-1,6-diphosphate. Enzyme activity was expressed in milliunits/mg protein. Protein content was assayed by the Lowry method [5]. The data were submitted to statistical processing, with use of Student's t criterion to evaluate mean differences.

Results and Discussion

The results listed in the Table indicate that aldolase activity in the ulnar bone was more than 5 times greater in rats decapitated 6-10 h after the spaceflight than in the vivarium control. There was less significant, but also reliable activation of aldolase at this time in rats used in the synchronous experiment.

On the 6th postexperiment day, aldolase activity diminished in bones of flight rats, but did not reach the control level; in the synchronous control, this parameter remained high and was double the value for the vivarium control.

The changes in aldolase activity in bones of rats submitted to repeated immobilization stress were different in the three experimental groups of animals. Thus, in vivarium control rats, there was no change in aldolase activity under the influence of immobilization stress, whereas in flight animals there was reliable increase in activity of this enzyme. In the synchronous experiment, this parameter decreased reliably after repeated stress, as compared to animals in the corresponding group who were not submitted to the stressogenic factor.

Immediately after landing, α-amylase activity in the ulna of flight rats was higher than in the synchronous experiment or vivarium control; however, in view of considerable individual variability of levels, this increase was not reliable. There was reliable decrease in activity of α-amylase in the vivarium control and synchronous experiment groups in response to the stressor effect of repeated immobilization.

As shown by our studies, maximum changes in activity of glycogenolytic enzymes in bone tissue were demonstrated in rats exposed to weightlessness. Similar changes, but less marked, were demonstrated in animals of the synchronous experiment. On this basis, it can be assumed that weightlessness does not

Activity of glycogenolytic enzymes in rat ulnar bone

TIME OF STUDY	STATIST INDEX	ALDOLASE, mU/MG PROTEIN			α-AMYLASE, mU/MG PROTEIN		
		ANIMAL GROUPS					
		FLIGHT	SYNCHRONOUS EXPERIMENT	VIVARIUM CONTROL	FLIGHT	SYNCHRONOUS EXPERIMENT	VIVARIUM CONTROL
6-10 H AFTER EXPERIMENT	$M \pm m$ n P_1	36,7±5,17 6 <0,001	11,6±0,46 6 <0,001	6,3±0,58 7 —	40,2±5,14 5 —	22,7±3,32 7 —	31,0±2,75 6 —
6TH DAY AFTER EXPERIMENT	$M \pm m$ n P_1	12,2±0,90 6 <0,01	13,4±0,91 5 <0,001	7,5±0,66 5 —	36,2±5,27 6 —	44,4±5,43 6 —	36,6±2,42 6 —
6TH DAY AFTER EXPERIMENT + REPEATED STRESS	$M \pm m$ n P_2	18,0±1,93 6 <0,05	6,3±0,59 7 <0,001	6,5±1,23 5 —	31,3±2,51 6 —	28,7±3,95 7 <0,05	25,0±3,82 7 <0,05

Key: P_1) reliability of differences as compared to vivarium control.
P_2) same as compared to corresponding group without repeated stress.

elicit specific changes in bone metabolism, and merely aggravates those induced by other spaceflight factors, which were simulated in the ground-based synchronous experiment.

As shown by the series of experiments with repeated immobilization, some changes in activity of glycogenolytic enzymes of bone tissue could occur in response to a non-specific stressogenic factor. In this case, however, there could be both activation and inhibition of glycogenolysis, and the nature of the response is apparently determined by the initial state of the enzyme systems at the time of exposure to the stressor agent.

The concurrent increase in activity of aldolase and α-amylase can be interpreted as indirect evidence of more intensive degradation of glycogen in the bone matrix of bones submitted to weightlessness. As has been indicated previously [4], the decrease in glycogen content of the bone matrix stimulates bone mineralization. Since there is a shift in the correlation between mineralization and demineralization processes in weightlessness, in the direction of prevalence of bone resorption, the demonstrated activation of enzymatic reactions of glycogenolysis in the bone matrix could be evaluated as a compensatory process aimed at attenuating the deleterious effect of weightlessness.

The submitted data warrant the conclusion that the 18.5-day spaceflight elicits in rats some changes in enzymatic activity of the organic bone matrix. The reaction of the enzymes studied, which are involved in degradation of glycogen, is probably directed toward elimination of the adverse effects of weightlessness.

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ORGANIC ACID PRODUCTION AND CARBONATE CONTENT OF RAT BONES AFTER SPACEFLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 25 Feb 82) pp 60-62

[Article by A. A. Prokhonchukov, K. S. Desyatnichenko and L. S. Kuznetsova]

[English abstract from source] The content of citric, pyruvic and lactic acids in bones of 30 rats flown on Cosmos-1129 was measured. Postflight the content of citric and pyruvic acids decreased and that of lactic acid increased. During readaptation the content of the acids tended to return to normal but never reached the vivarium level. The mechanism of these changes is discussed.

[Text] The role of organic acids in mobilizing minerals deposited in skeletal bones has attracted the attention of researchers for a relatively long time [1-3]. However, the existing information about the nature of their effect on bone metabolism is contradictory [4, 5], and it does not enable us to unequivocally determine their relevance to physiological function of the skeleton in maintaining mineral homeostasis and pathological demineralization of hard tissues. The question of involvement of organic acids in the mechanism of skeletal decalcification under the effect of hypokinesia and weightlessness has also been insufficiently investigated.

We submit here data on levels of citrate, lactate and pyruvate in bones of rats flown for 18.5 days in Cosmos-1129 biosatellite, animals used in a ground-based synchronous experiment and vivarium control (6-7 animals per group). We assayed in the same bone samples carbonate, which could be used, by virtue of its acid-lability, as an indicator of the demineralizing effect of organic acids [6].

Methods

Preparation of bones for biochemical analyses was described previously [7]. To assay citrate content, we used a hydrolysate of bone power incubated in 6 N HCl at a temperature of 105°C for 18 h. It was established in preliminary experiments that such treatment provides 95% yield of citric acid, and it permits concurrent preparation of samples for assaying hydroxyproline and tyrosine, which are indicators of collagen and noncollagen proteins. Analysis was performed

with a modified method: bromated citrate and colorimetry of the complex of pentabromacetone with thiourea in a mildly alkaline medium [8].

For assays of lactate and pyruvate, bone power was extracted with 1/15 M phosphate buffer, pH 7.4 (10 mg/mℓ) followed by precipitation of proteins. Pyruvate was assayed in the protein-free extract by the method of Umbright as modified by O. M. Babaskin [9] and lactate according to Berker and Sammerson [10].

Carbonate content of bones was assayed by measuring the amount of carbon dioxide driven out by H_2O_4, in Conway paraffin diffusion chambers. CO_2 was absorbed with 0.2 N KOH placed in the inside container of the chamber, and it was measured by the difference in pH of KOH solution placed in a control (empty) and experimental chambers. Alkali solutions for plotting the calibration curve were prepared after titration of the initial solution with 0.1 N HCl.

Results and Discussion

Organic acid and carbonate content of bones of rats kept in the vivarium (see Table) was close to the levels cited in the literature [11-13]. These parameters underwent considerable changes under the influence of spaceflight conditions, as well as hypokinesia in the synchronous experiment, and it consisted of decline of citric acid and pyruvate levels with concurrent elevation of lactate.

Organic acid and carbonate content of rat bone tissue

TIME OF STUDY	CITRIC ACID	PYRUVATE	LACTATE	LACTATE/PYRUVATE COEFFICIENT	CO_3^{2-}, MEQ/100 G DRY DEFATTED BONE
	IN MMOL/100 G DRY DEFATTED BONE				
FLIGHT					
IMMEDIATELY AFTER FLT	5,00±0,67*	0,09±0,02*	13,66±1,19*	151,8	54,7±15,7*
AFTER READAPTATION	8,67±0,44	0,16±0,01*	10,35±0,41	64,7	114,5±23,8
SYNCHRONOUS EXPERIMENT					
IMMEDIATELY AFTER	5,44±1,11*	0,08±0,01*	12,02±0,64*	150,3	53,5±10,9*
AFTER READAPTATION	10,67±0,89	0,24±0,02	12,72±0,53*	53,0	106,1±20,4
VIVARIUM CONTROL	10,28±0,28	0,28±0,01	8,74±0,22	31,3	144,2±12,2

*Values differing from corresponding parameters in the vivarium control with at least 95% level according to the criterion of Wilcoxson-Mann-Whitney.

Under physiological conditions, up to 90% of the body's citrate is deposited in the skeleton [1], where it is firmly bound with the mineral phase [2, 14]. For this reason, the decline of its level can be interpreted as an indication of change in carbohydrate metabolism only with great caution. It is more likely related to mobilization from the skeleton. In contrast, the increase in lactate/pyruvate coefficient can be interpreted as intensification of glycolytic activity and decrease in aerobic oxidation of carbohydrates. This conclusion conforms entirely to previous findings concerning impaired oxygenation and metabolic changes during spaceflights.

As was demonstrated previously [7], rat bone tissue was partially demineralized after 19-day spaceflight, mainly referable to the fraction of amorphous calcium phosphate. Can the changes described here in chemical composition of the organic phase of bone be related to decalcification? The elevation of lactate level in bone was far from being equivalent to decline of tribasic citric acid (see Table). Yet it is known that, with increase in alkalinity of acid there is increase in its affinity for Ca^{2+} [2]. It is also believed that citrate plays an important part in mobilizing bone tissue calcium [1, 5]. On the other hand, there are reports to the effect that bone resorption elicited by parathyroid hormone is not attributable to its effect on citrate metabolism, but to intensification of glycolysis [3], as well as that citric acid can accumulate in bone without causing its resorption [15].

Assay of carbonate in bones revealed that its level dropped significantly in bone tissue of experimental groups of animals (see Table). This warrants the belief that there is tissular acidosis in decalcified bone. The change in acid-base equilibrium, as well as activation of glycolysis, could be due to the effect of parathyroid hormone on osteogenic cells [15, 16]. The amount of carbon dioxide released from bone is greater by a factor of 10^1 than the demonstrated organic acids. Perhaps, part of the carbonate groups of apatite was isomorphously replaced by hydroxyl groups. This oxidizes the medium additionally.

The above contradictions in interpreting the role of citric acid can probably be also attributed to conditions of acid-base equilibrium. The following experiment was conducted to confirm this thesis. Samples of the dog's tibia, which were decalcified in EDTA [ethylenediamene tetraacetate], were incubated for 2 h in 0.1 M citric acid solutions containing $^{45}CaCl_2$ in a concentration of 5 meq/ℓ with ^{45}Ca activity of 706,000±980 counts/min/mℓ. The pH of this solution was brought to 6.0 for one of the series of matrix samples and to 7.5 for another by means of concentrated alkali. After incubation, the matrix samples were eluated for 2 h in 5 changes of double-distilled water, dried to a constant mass, dissolved by heating in perchloric acid and their radioactivity was measured using a Mark-2 (Searle Co., United States) liquid-scintillation counter.

It was found that the radioactivity of pieces of matrix incubated at pH 6.0 did not exceed background levels, whereas analogous specimens incubated at pH 7.5 bound 10.5±0.3 meq Ca^{2+}/g dry tissue (scaled to radioactivity of ^{45}Ca in counts/min/mℓ for Ca^{2+} concentration, in microequivalents). This level showed virtually no difference from the Ca-binding capacity of organic bone matrix, as established by the above-described method but with use of tris-HCl buffer, pH 7.5, with the same proportion of ^{45}Ca and its stable isotope. Incubation of the matrix prelabeled with ^{45}Ca in a citrate solution, pH 6.0, led to decline of its activity to the base level. Thus, it can be considered that with pH in the physiological range the affinity of bone matrix for calcium is greater than that of citric acid, and under these conditions citrate can play the role of Ca^{2+} in the process of mineralization. The decrease in its level in the bone specimens examined is probably attributable to production of soluble, unsubstituted salts of Ca citrate that pass into tissular fluid and the blood stream.

The tested parameters demonstrated considerable normalization (see Table) during the recovery period, in both animals flown aboard Cosmos-1129 and rats

used in the synchronous experiment, which is indicative of high metabolic activity of bone tissue and presence in it of large functional and plastic reserves.

In conclusion, it should be noted that the above interpretation of the mechanism of bone decalcification under the effect of spaceflight factors is by no means in contradiction with a hypothesis we expounded previously [7] concerning the role of impaired bonds in the protein-calcium-phosphate complex in this process. Both phenomena (proteolysis and tissular acidosis) may be due to the same cause--impaired tissular oxygenation--and they can occur simultaneously. Perhaps, halisteresis under the effect of organic acids prepares the way for and facilitates proteolysis.

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EFFECT OF LONG-TERM HYPOKINESIA ON THYROID C CELLS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 14 May 82) pp 63-66

[Article by G. I. Plakhuta-Plakutina]

[English abstract from source] The state of C-cells of the thyroid gland of Wistar rats during prolonged (30-165 days) hypokinesia was examined. Histo- and morphometric data pointed to a gradual decline in the function of C-cells during hypokinesia and its return to normal after 2-month readaptation. The decline was most distinct by hypokinesia day 90 (significant decrease in the number and size of nuclei, prevalence of small cells with densely packed granules in the cytoplasm). The decline in the function of C-cells during hypokinesia may be one of the factors leading to increased calcium elimination from bones. In conclusion, the state of C-cells in animals exposed to weightlessness and hypokinesia is compared.

[Text] Most morphological studies deal with the specific investigation of reactions of calcitonin-producing cells of the thyroid to models of hypercalcemia and hypocalcemia produced by exogenous interventions [1-3]. Such studies had not been conducted with use of experimental factors associated with impairment of calcium metabolism (for example, hypokinesia). Yet we had demonstrated that exposure of animals to weightlessness causes a decrease in functional activity and number of C cells. The same direction of changes in bone tissue and calcium metabolism in weightlessness and under hypokinetic conditions served as grounds for investigating the system of C cells during prolonged hypokinesia.

Methods

Experiments were conducted on 84 male Wistar rats with initial weight of 270-300 g. Hypokinesia was produced by using special box-cages made of plexiglas, which restricted considerably the animals' motor activity. Hypokinesia lasted 30 to 165 days. Rats kept in larger cages served as a control. For histological and morphometric studies, we took the thyroid and parathyroid glands from 6 rats in the control and experimental groups, who were sacrificed by ether anesthesia on the 30th, 60th, 90th, 120th and 165th day of hypokinesia, as well as 2 and

3 months after 165-day hypokinesia. Six intact animals were sacrificed on the day we started the experiment in order to obtain background data (basic control).

Thyroid glands were fixed in Bouin fluid and imbedded in paraffin. Sections were stained with hematoxylin-eosin, light green, according to Helmy. C cells were demonstrated by the method of Grandi. We determined the volume of nuclei of C cells and parathyrocytes by means of RA-6 at 2000× magnification, for which purpose we sketched the outline projections of 100 nuclei and determined the logarithms of their volumes from the Fisher and Inkle nomogram. In all, we measured 9000 nuclei. We counted C cells using an ocular grid at 7×40 magnification by the random sample method in 10 grids. We used the Student-Fisher criterion for statistical processing of digital data.

Results and Discussion

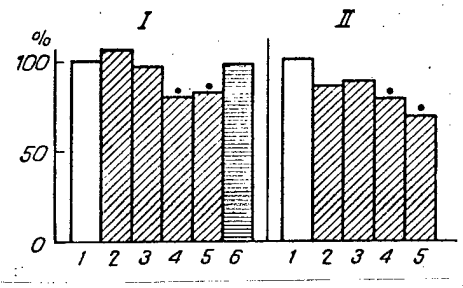
During the 165-day experiment, as the control group of rats grew older and gained weight, the absolute mass of the thyroid also increased. The increment in gland weight, as compared to the basic, initial level, was particularly significant in the 3d (21%) and 5.5th month (25%). In experimental animals, against a background of weight loss and inhibition of linear growth (in particular, of the tail), the absolute mass of the thyroid remained close to that of the basic control to the end of the experiment, i.e., it did not increase in the course of 5.5 months of hypokinesia. For this reason, starting in the 2d and particularly during the 3d month of hypokinesia, we observed reliable decrease in absolute thyroid mass, as compared to the corresponding control.

Let us dwell in greater detail on the dynamics of changes in the system of C cells, since their state had not been studied under hypokinetic conditions. In control animals, C cells were well demonstrable in preparations stained with hematoxylin-eosin, as well as impregnated with silver. The number of C cells held at the same level for the first 2 months (134.0±7.0 and 129.0±8.4), but increased significantly after 3 months (192.0±9.8) and remained the same after 5.5 months (194.0±18.0). The volume of C cell nuclei also had a tendency toward increasing with age: it constituted 107.9±4.3 μm^3 in the 1st month and 121.5±4.5 μm^3 in the 5th. There are reports in the literature concerning overall increase in quantity of C cells and TKT hormone [thyrocalcitonin?] in the rat's gland as they grow older [4, 5].

At all tested times, most intact animals demonstrated C cells at different stages of the secretory cycle, as could be determined from the degree of filling of cytoplasm with secretory granules. The C cells (mainly large ones) presented epifollicular and parafollicular localization, forming accumulations (of 5-7 cells each) in interfollicular tissue.

At the first stage of hypokinesia (1-2 months), C cells were well-demonstrable with usual staining methods. On sections impregnated by the method of Grandi, as in the control, there was prevalence of cells whose cytoplasm was filled with many secretory granules varying in size and density. We often encountered cells with "loose" distribution of granules, or else the granules appeared to go beyond the limits of cytoplasm. At the same time, we were able to detect appearance of small cells with narrow bands of cytoplasm filled with fine, dark granules. Such cells were strongly impregnated, acquiring an elongated,

fusiform shape. At this stage of hypokinesia the number of C cells tends to diminish (by 12-16%, P = 0.05), but the size of the nuclei does not differ reliably from the control.



Dynamics of changes in volume of C cell nuclei (I) and number (II). The dots point to statistically reliable differences from control

1) control
2-5) 30th, 60th, 90th and 165th days, respectively, of hypokinesia
6) 60th day after 165 days of hypokinesia

After 3 months, there was substantial decrease in number of C cells in experimental animals, as compared to the control (146.0±9.9, versus 192.0±9.8); however, as in intact rats of this age, their number increases significantly, as compared to the preceding stage, and this can be attributed to growth changes. There was concurrent reduction in nucleus size (by 23%, as compared to control, P<0.01). We demonstrated many small, seemingly flattened fusiform cells with small nuclei and collapsed cytoplasm containing dark, consolidated granules. In addition, we encountered some poorly impregnated cells with diffuse outlines and signs of degranulation. Such cells are difficult to demonstrate with the usual stains, their cytoplasm becomes clear and faintly colored.

In the 4th and 5.5th months of hypokinesia, the above changes in C cells persisted and progressed. Signs of degranulation were accompanied by dystrophic changes in cells (appearance of "shadow cells," vacuolization of cytoplasm, karyorrhexis). There was also an increase in quantity of "collapsed" cells, which were notable for their small nuclei and cytoplasm. This led to further decrease in number of C cells, as compared to both the preceding stage and, particularly, the corresponding control (at 5.5 months, 126.0±11.0 in the experiment versus 194.0±18.0 in the control). The size of the nuclei also remained diminished (95.0±7.0, versus 121.5±4.5 in the control). At the same time, at all stages of the experiment there were preserved groups of cells, whose size, shape and granule content were the same as in intact animals.

Two months into the recovery period, the animals were still behind in growth, but absolute and relative mass of the thyroid was close to the control. The population of C cells revealed a state that was typical in control animals. The Figure illustrates the number of C cells and volume of their nuclei in experimental animals (as percentage of corresponding control data).

Thus, while we observed a tendency toward reduction of the C-cell population in the 1st-2d months of the experiment, by the 3d month of hypokinesia both the quantity and size of C cells diminished reliably and remained low to the end of the hypokinetic period. There was prevalence of collapsed cells that were small and had densely arranged granules in the cytoplasm, which were apparently functionally inactive. According to data in the literature, such morphological changes in C cells are observed at the late stages of hypercalcemia [2] and they reflect the phase of "depletion" of this system.

The described histlogical and morphometric signs are indicative of gradual decline of parafollicular system function during hypokinesia. Perhaps, decline or attenuation of functional activity of C cells is instrumental in development of the changes observed in bones during hypokinesia. Studies that demonstrated that exogenously administered thyrocalcitonin during hypokinesia leads to attenuation of resorptive processes in bone tissue can serve as confirmation of this [6, 7]. The question of condition of parathyroid glands during hypokinesia obviously arises because of the antagonistic correlations between calcitonin and parathyroid hormone.

Histological examination of parathyroid glands in the course of 165-day hypokinesia failed to demonstrate any structural distinctions. As in the control, the glands were large, their parenchyma was represented by parathyrocytes differing in size and shape. Morphometry of nuclei of the chief parathyrocytes failed to reveal changes in their volume throughout the experiment.

Studies of the parathyroid using light and electron microscopy in rats with an immobilized limb for both a short (9 weeks) and long (up to 4.5 months) time failed to demonstrate appreciable changes in activity of this gland, although there was retardation of weight gain, decrease in density and marked atrophy of the limb in experimental animals [8, 9]. At the same time, experiments with dogs revealed that no signs of osteoporosis in the immobilized limbs developed after removal of the thyroid and parathyroid [10]. Consequently, the absence of morphological signs of increased functional activity of the parathyroid during immobilization and hypokinesia does not rule out its involvement in processes of impairment of calcium metabolism in these experiments.

The results of previous studies on biosatellites revealed that animals exposed to weightlessness presented a decrease in number and volume of nuclei and C cells in the thyroid, whereas focal hypertrophy of parathyrocytes was observed in the parathyroid [11, 12].

Since there was focal hypertrophy of parathyrocytes in animals exposed to weightlessness, it can be assumed that the degree of activation of parathyroid function is determined by the extent of decline of load on the skeletomuscular system. The results obtained from studies of C cells of animals flown in biosatellites and in this experiment are indicative of similar changes in this system [in the same direction]. However, the rate and severity of these changes in the C cell population were not the same. Signs of depression of C-cell functional activity appeared on the 18th-22d day of flight in weightlessness, whereas with hypokinesia they appeared by the 90th experimental day.

Thus, when the support function is taken away from the skeleton in weightlessness, the decline in C-cell function is combined with focal hypertrophy of parathyrocytes, while the underload on the skeletomuscular system during hypokinesia elicits hypofunction of C cells without morphological signs of activation of parathyroid glands, and in both cases this could serve as one of the causes of increased mobilization of calcium from bones.

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COMPLEMENT AND HETEROPHIL ANTIBODY LEVELS IN MONKEYS DURING ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 2 Mar 82) pp 66-67

[Article by A. A. Ivanov, V. N. Shvets and M. I. Boyko]

[English abstract from source] The experiments with sexually immature (about 3 years) primates Macaca mulatta exposed to head-down tilt and clinostating hypokinesia showed an increase in the complementary activity of serum and a decrease of heterophil antibodies in the first case. It is inferred that an increase in the complement content reflects an adaptive reaction to head-down tilt and a decrease in heterophil antibodies indicates an inhibition of antibody-forming cells (B lymphocytes).

[Text] In our previous studies we demonstrated that, during horizontal hypokinesia [1], as well as spaceflight [2], rats present elevation of blood serum complement level and less significant change in level of heterophil antibodies to ram erythrocytes.

Our objective here was to investigate the immunity system of primates during antiorthostatic [head-down tilt] hypokinesia.

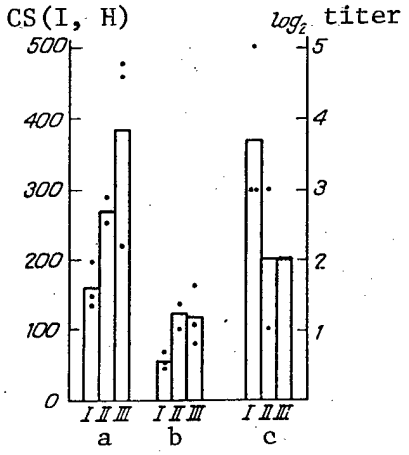
Methods

This study was conducted on 8 impuberal (about 3 years old) Macaca mulatta male monkeys weighing 3-4 kg. The animals were divided into three groups: the first consisted of 3 healthy, intact animals; the second of 2 monkeys who spent 2 days in a primatological chair then 7 days in antiorthostatic head-dwon (-6°) position; the third group consisted of 3 monkeys first submitted to clinostatic hypokinesia for 7 days then antiorthostatic position for 12 days, under the same conditions as the second group. The animals were sacrificed by intravenous injection of 2.5-3.0 mℓ 10% hexenal solution, which caused immediate respiratory and cardiac arrest. Blood serum complement level was assayed by a kinetic method [3], which enabled us to assess complement activity of blood serum according to two parameters: reciprocal of induction period (in kinetic units of complement for induction period) and rate of hemolysis (in kinetic units of rate of hemolysis).

The titer of heterophil antibodies (hemagglutinins) was determined with a Takachi microtitrator [1] using 2% suspension of ram erythrocytes.

Results and Discussion

The data illustrated in the Figure demonstrate convincingly the strong effect of antiorthostatic hypokinesia on the parameters studied. The experimental groups of animals demonstrated a marked increase (statistically reliable according to the T criterion of White [5], as compared to control values and combined sample of experimental groups) complement activity of blood serum, as determined both by the duration of the induction period ($p = 0.05$) and rate of hemolysis (see Figure, a and b). Conversely, heterophil antibody level was lower in experimental groups of animals.



Complement level determined by kinetic method according to induction period (a), rate of hemolysis (b) and heterophil antibodies (c) in control group (I) of monkeys, after 7-day (II) and 19-day (III) hypokinesia [CS--complement system] Dots show individual values of parameters.

Considering the well-known facts concerning involvement of the complement system in various physiological processes, we previously expounded the hypothesis that the decrease in muscular activity during hypokinesia causes accumulation and decreased expenditure of complement in the body [1] and in rate of its catabolism. On the other hand, it is known that various stress factors (excitation of nervous system, thermal burn, irradiation, infection, etc. [4]) cause early elevation of complement level.

It can be assumed that, in our experiment, the increase in complement content of blood reflects the body's adaptive reaction to hypokinesia, and in this respect it is a nonspecific defense factor.

The nature of changes in levels of heterophil antibodies was just the opposite of changes in complement level (see Figure, c), which is indicative of diminished function of antibody-producing cells (B lymphocytes) during antiorthostatic hypokinesia.

Thus, this experiment with primates revealed that there is appreciable rise of complement level and decline of heterophil antibodies during head-down hypokinesia. These data confirm the general direction of changes in these parameters under hypokinetic conditions, as well as under the effect of spaceflight factors [1, 2].

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TRICARBOXYLIC ACID CYCLE OXIDATIVE ENZYME ACTIVITY IN LIVER OF HYPOKINETIC RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 9 Mar 82) pp 67-71

[Article by Yu. A. Ganin]

[English abstract from source] The activity of oxidative enzymes of the Krebs cycle was examined in white rats during hypokinesia. On hypokinesia day 7 the cytosol activity of NAD-dependent isocitrate dehydrogenase (ICDH) increased and that of malic enzyme decreased. On hypokinesia days 30 and 45 the activity of succinate dehydrogenase (SDH) and α-ketoglutarate dehydrogenase (α-KGDH) decreased, that of cytoplasmatic malate dehydrogenases (MDH) slightly increased, and that of NADP ICDH declined. On hypokinesia day 60 the total activity of mitochondrial dehydrogenases reduced due to a low protein content of the mitochondrial fraction, whereas the specific activity either remained unchanged (ICDH, NAD MDH, α-KGDH) or increased (SDH, NADP MDH). On recovery day 25 only the activity of mitochondrial NAD-dependent malate and isocitrate dehydrogenases returned to normal.

[Text] Hypokinesia and weightlessness, as spaceflight factors, elicit substantial changes in metabolism and functions [1-4], and maximum changes were demonstrated in skeletal muscles and the myocardium. Liver metabolism has been studied less. Energy metabolism is significantly impaired when movement is restricted [11]; however, virtually no studies have been made of change in activity of oxidative enzymes of the Krebs cycle (KC).

We report here on our study of activity of mitochondrial and cytoplasmic forms of NAD- and NADP-dependent isocitrate dehydrogenases (ICDH) and malate dehydrogenases (MDH), succinate dehydrogenase (SDH) and α-ketoglutarate dehydrogenase (KGDH).

Methods

The studies were conducted with 64 control and 68 experimental male rats with initial weight of 160-170 g. Their movement was restricted by keeping them in small individual box-cages made of plexiglas. The animals were decapitated on the 7th, 30th, 45th and 60th days of the experiment and 25th day of the

Table 1. ICDH activity in mitochondrial and cytoplasmic fraction of liver of hypokinetic rats

ENZYME STUDIED	ANIMAL GROUP	DAY OF HYPOKINESIA				RECOVERY PERIOD (25TH DAY)
		7	30	45	60	
SPECIFIC MITOCHONDRIAL NAD ICDH ACTIVITY, NM/MG PROTEIN/MIN	CONTROL	3,6±1 (7)	3,8±0,2 (8)	5,0±0,2 (7)	3,4±0,1 (7)	3,7±0,3 (6)
	EXPERIM.	5,8±0,3 (7)*	4,1±0,3 (7)	4,6±0,3 (7)	3,1±0,2 (7)	3,9±0,3 (6)
OVERALL MITOCHONDR. NAD ICDH ACTIVITY, NM/G TISSUE/MIN	CONTROL	72±3 (7)	74±3 (8)	120±8 (7)	92±2 (7)	79±8 (6)
	EXPERIM.	131±7 (7)*	87±5 (7)*	97±7 (7)*	65±6 (7)*	77±8 (6)
SPECIF. MITOCHONDR. NADP ICDH ACTIVITY, NM MG/PROTEIN/MIN	CONTROL	45±1 (7)	47±2 (8)	45±3 (7)	42±3 (7)	32±2 (6)
	EXPERIM.	42±1 (7)	52±3 (7)	50±3 (7)	44±3 (7)	45±2 (6)*
OVERALL MITOCHONDR. NADP ICDH ACTIVITY, NM/G TISSUE/MIN	CONTROL	936±34 (7)	1017±79 (8)	1042±90 (7)	1038±85 (7)	678±65 (6)
	EXPERIM.	968±47 (7)	1130±73 (7)	1061±93 (7)	881±63 (7)	861±58 (6)*
OVERALL CYTOSOL NADP ICDH ACTIVITY, µM/G TISSUE/MIN	CONTROL	11,9±0,43 (7)	14,3±1,06 (8)	16,3±0,66 (7)	12,1±0,29 (7)	14,9±0,76 (6)
	EXPERIM.	11,6±0,34 (7)	13,7±54 (7)	13,2±0,34 (7)*	10,35±0,72 (7)*	12,2±0,62 (6)*

Note: Here and in Tables 2 and 3, number of animals in group is given in parentheses. $P<0.05$ is marked with an asterisk.

recovery period after 60-day hypokinesia. We took for examination hepatic tissue (about 1.5 g) from the anterior edge of the right lobe without ligaments or fascia. The mitochondrial fraction and the fraction containing soluble cytoplasm were recovered by differential centrifugation according to Garland [5] and Sottocasa [6] in a cold room at 0-4°C. Isolation media contained 0.25 M saccharose, 0.05 M tris buffer, 0.005 M $MgCl_2$, 0.001 M EDTA [ethylenediamine tetraacetate], pH 7.4. To solubilize and stabilize enzymes, we used a medium proposed by Watanabe [18]. Purity of the mitochondrial fraction was checked by means of marker enzymes [8]. Activity of malate and isocitrate dehydrogenases was measured by spectrophotometry according to formation of reduced forms of pyridine nucleotides in the incubation media described for NAD-dependent ICDH (NAD ICDH; EC 1.1.1.41) by Plaute [9], for NADP-dependent ICDH (NADP ICDH; EC 1.1.1.42) by Salganicoff and Koeppe [10], for NAD-dependent MDH (NAD MDH, EC 1.1.1.37) by Ochoa [11] and for NADP-dependent MDH ("malic" enzyme, NADP MDH; EC 1.1.1.40) by Brdiczka and Pette [12]. Activity of SDH (EC 1.3.9.91) and KGDH (EC 1.2.4.2) was determined in the reaction with dichlorphenolindophenol [dichloroindophenol] as electron acceptor [8]. Protein was assayed by the method of Lowry as described by A. A. Pokrovskiy [13]. We calculated specific (per mg mitochondrial protein) and overall (per gram wet tissue) activity of mitochondrial enzymes. We calculated only activity per gram tissue for the cytoplasmic forms of NAD MDH, NADP MDH, and NADP ICDH. Specific activity of these enzymes was not analyzed, in view of the heterogeneity of the protein composition of the supramitochondrial fraction.

Results and Discussion

Table 1 lists the changes in ICDH activity. NAD ICDH is a regulatory enzyme whose activity is controlled by the $NAD/NAD \cdot H_2$

ratio and relative amount of ADP in the total amount of adenylic nucleotides. Under physiological conditions, this reaction is irreversible [14], its rate increases with increase in concentration of cAMP and isocitrate [9]. We demonstrated an increase in NAD ICDH activity on the 7th day of hypokinesia (by 61% for specific activity and 82% for overall activity). Since the share of NAD-dependent oxidation of isocitrate constitutes only 2-3% in the liver, this increase could not cause appreciable increase in flow of metabolites in KC. Probably, in this instance the parameter depends on changes in enzyme activators and inhibitors. Several authors [15] have demonstrated an increase in cAMP at the short term of immobilization. The increase in oxidation of pyridine nucleotides could be another factor that increases activity of this enzyme. By the 45th experimental day, overall activity of the enzyme decreased by 19.2% and by the 60th day, by 29%, which reflects a tendency toward decrease in intensity of oxidative processes in KC at these times. This phenomenon was associated with an 18.5% decrease in protein content of the mitochondrial fraction.

NADP ICDH catalyzes a reversible reaction both in mitochondria and cytoplasm, and activity of the enzyme depends on the quantity and availability of substrate. We failed to demonstrate appreciable changes in activity of mitochondrial NADP ICDH at different stages of hypokinesis, whereas cytoplasm revealed a 19% decrease in activity on the 45th day and 15% decrease on the 60th day. Predominant use of citric acid for degradation in the citrate-lyase reaction, which initiates lipogenesis [16], intensification of which has been demonstrated under hypokinetic conditions [17], rather than for oxidation and maintenance of the required NADP/NADP$\cdot H_2$ level, could be the cause of such changes.

On the 25th day of the recovery period, activity of NAD ICDH did not differ from the control; mitochondrial NADP ICDH activity increased reliably by 27%, whereas the cytoplasmic form constituted 8.14% of the control. The role of NADP ICDH in the cell consisted primarily of implementing NADP$\cdot H_2$ reduced synthesis. The increase in activity of the enzyme in mitochondria was indicative of build-up of these processes expressly in mitochondria. At this time, the pool of NADP$\cdot H_2$ in cytoplasm was supplied mainly as a result of acceleration of pentose pathway reactions [17].

Table 2 lists data on the effect of hypokinesia on MDH activity. Mitochondrial NAD MDH activity was somewhat diminished (14.3%) only on the 30th day. Such findings had been made [18] for MDH in a liver homogenate. Activity of the cytoplasmic form of the enzyme increased appreciably on the 45th day (by 27.4%). Cytosol NAD MDH was 28.3% lower than the control in the recovery period.

Judging from its activity, NAD MDH is the most "powerful" enzyme of the KC, and only 2-5% of its activity is expended for oxidation of metabolites proper of this cycle. The main function of the enzyme is its involvement in exchange of reduced equivalents between mitochondria and cytoplasm [19]. The change in cytosol NAD MDH/mitochondrial NAD MDH activity ratio could reflect, to some degree, impairment of this process. On the 30th, 45th and 60th days of hypokinesia this parameter increased; it did not change on the 7th day, whereas in the recovery period it diminished, which could be related to change in substrate supply of the KC at this time.

Table 2. Malate dehydrogenase activity in mitochondrial and cytoplasmic liver fraction in hypokinetic rats

ENZYME STUDIED	ANIMAL GROUP	DAY OF HYPOKINESIA 7	30	45	60	RECOVERY PERIOD (25TH DAY)
SPECIF. MITOCHONDR. NAD MDH ACTIVITY, NM/MG PROTEIN/MIN	CONTROL	396±15 (7)	447±17 (8)	539±35 (7)	296±21 (9)	389±22 (6)
	EXPERIM.	369±26 (7)	388±18 (7)*	579±38 (7)	311±18 (7)	399±28 (6)
OVERALL MITOCHONDR. NAD MDH ACTIVITY, μM/G TISSUE/MIN	CONTROL	8,70±0,42 (7)	9,59±0,54 (8)	12,5±1,06 (7)	7,28±0,65 (9)	8,10±0,24 (7)
	EXPERIM.	8,40±0,66 (7)	8,22±0,32 (7)*	12,2±1,12 (7)	6,24±0,48 (7)	7,97±0,84 (6)
OVERALL CYTOSOL NAD MDH ACTIVITY, μM/G TISSUE/MIN	CONTROL	162,5±6,0 (7)	165,1±5,3 (8)	171,2±3,0 (7)	138,9±5,9 (9)	214,5±18,5 (6)
	EXPERIM.	154,4±3,0 (7)	169,8±9,2 (7)	218,2±10,1 (7)*	141,4±22,0 (7)	153,7±18,6 (6)*
SPECIF. MITOCHONDRIAL NADP MDH ACTIVITY, NM/MG PROTEIN/MIN	CONTROL	2,6±0,1 (7)	2,7±0,2 (8)	2,9±0,2 (7)	2,6±0,1 (8)	3,4±0,1 (6)
	EXPERIM.	2,2±0,2 (7)	3,0±0,3 (7)	3,4±0,3 (7)	3,5±0,3 (7)*	3,1±0,2 (6)
OVERALL MITOCHONDR. NAD MDH ACTIVITY, μM/G TISSUE/MIN	CONTROL	53±3 (7)	57±4 (8)	70±5 (7)	65±3 (8)	74±4 (6)
	EXPERIM.	49±4 (7)	64±6 (7)	62±5 (7)	68±5 (7)	62±6 (6)
OVERALL CYTOSOL NADP MDH ACTIVITY, NM/G TISSUE/MIN	CONTROL	2113±62 (7)*	1806±16 (8)	1457±85 (7)	1320±100 (8)	1130±32 (7)
	EXPERIM.	1103±42 (7)	1536±145 (7)	1617±103 (7)	1534±118 (7)	2066±202 (6)*

Table 3. Succinate dehydrogenase and α-ketoglutarate dehydrogenase activity in rat liver mitochondria at different stages of hypokinesia (in nM substrate/min)

PARAMETER STUDIED	ANIMAL GROUP	DAY OF HYPOKINESIA 7	30	45	60	RECOVERY PERIOD (25TH DAY)
SPECIFIC SDH ACTIVITY	CONTROL	122±3 (7)	120±4 (8)	116±5 (7)	73±5 (10)	121±6 (6)
	EXPERIM.	136±9 (7)	102±5 (7)*	92±4 (7)*	92±8 (7)*	98±8 (6)*
OVERALL SDH ACTIVITY	CONTROL	2553±101 (7)	2592±127 (8)	2695±96 (7)	1812±173 (10)	2521±118 (6)
	EXPERIM.	2947±234 (7)	2194±130 (7)*	1938±129 (7)*	1840±220 (7)	1967±177 (6)*
SPECIFIC KGDH ACTIVITY	CONTROL	87±4,5 (7)	84±4,2 (8)	78±4,8 (7)	47±2,8 (10)	83±6 (6)
	EXPERIM.	80±4,7	71±5,3 (7)	58±3,7 (7)*	53±5,2 (7)	61±4 (6)*
OVERALL KGDH ACTIVITY	CONTROL	1822±90 (7)	1800±104 (8)	1810±110 (7)	1209±83 (10)	1730±94 (6)
	EXPERIM.	1884±200 (7)	1527±151 (7)	1232±92 (7)*	988±66 (7)*	1225±125 (6)*
MITOCHONDRIAL FRACTION PROTEIN, MG/G TISSUE	CONTROL	21,1±0,41 (7)	19,4±1,02 (8)	23,3±1,10 (7)	24,5±0,84 (10)	21,0±0,88 (6)
	EXPERIM.	22,6±1,95 (7)	21,3±0,82 (7)	20,9±0,64 (7)	20,0±1,07 (7)*	19,8±1,02 (6)

NADP MDH is not referable to KC enzymes, but it catalyzes the conjugate reaction of reducing carboxylation of pyruvate, increasing the stock of dicarboxylic acids. The role of this enzyme is closely linked to the function of the citrate-pyruvate cycle [20] and initial stages of gluconeogenesis [12]. The decline (by 47.8%) of its activity in cytoplasm on the 7th day of immobilization is attributable mainly to oxidation of carbohydrates, intensive degradation of glycogen [21] and hyperglycemia [4], whereas prolonged hypokinesia apparently depletes the glycogen supply [21] due to activation of fatty acid breakdown [17], which must lead to intensification of gluconeogenesis and synthesis of dicarboxylic acids from pyruvate. The experiments revealed that extension of the hypokinetic period was associated with gradual increase in activity of the "malic" enzyme; the increase in NADP MDH activity of cytosol was at a maximum--by 82.6%--in the recovery period.

SHD activity (Table 3) was diminished on the 30th and 45th day with reference to specific activity. By the 60th day, overall activity of the enzyme did not differ from the control, since the 26% increase in specific activity compensated for the low mitochondrial protein content.

Analogous changes were demonstrated in KGDH. By the 30th day, overall activity of this enzyme decreased by 15.5% and by the 45th day, by 25.7% however, the increase in specific activity was insignificant by the 60th day. Overall activity was 19.3% lower than in the control.

In the recovery period, activity of both SDH and KGDH was diminished, by 22 and 29.2%, which was attributable to specific activity, since there was normalization at this time of mitochondrial fraction protein content.

Of all the enzymes studied, only NAD ICDH and NAD MDH of mitochondria failed to undergo changes by the 25th day of the recovery period. Apparently, this was not a long enough recovery period for complete readjustment to a normal regimen of motor activity.

On the whole, the changes under hypokinetic conditions were less marked in the liver than in contractile tissues [22].

Thus, our investigation enabled us to assess disturbances of oxidative processes in the Krebs cycle at different stages of immobilization, and it has expended appreciably the existing information about metabolic disturbances associated with hypokinesia.

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EXCRETION OF EPINEPHRINE AND NOREPINEPHRINE IN URINE IN PRESENCE OF PRESSURE-CHAMBER HYPOXIA IN MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 1 Apr 82) pp 71-75

[Article by I. P. Yakovleva, I. S. Balakhovskiy, V. N. Polyakov, V. K. Stepanov and M. V. Dvornikov]

[English abstract from source] The effect of altitude chamber hypoxia of different intensity and duration on epinephrine and norepinephrine excretion was investigated. The hypoxia tolerance as a function of catecholamine excretion was also examined. At altitudes 5000 and 6500-7000 m the test subjects were kept for a short time and at 3500-4500 m for 24 hours. The subjects with high hypoxia tolerance showed an increased and those with low tolerance a decreased epinephrine excretion. The epinephrine excretion did not increase with the intensity and duration of the hypoxia effect. Variations in the norepinephrine excretion were insignificant in all tests.

[Text] It is known that, in a number of instances, hypoxia is associated with a marked reaction by the adrenosympathetic system [1, 2]. However, neither its pathogenesis nor role in assuring resistance to oxygen deficiency can be considered completely determined. Most often, an increase in pyrocatechin levels in blood and their excretion in urine was observed during ascents in the mountains [3-5]. In the case of pressure-chamber hypoxia, a reaction is demonstrable in some instances [6, 7] and not in others [8, 9]. It is difficult to settle this matter because the effect of hypoxia is almost inevitably associated with other factors: hypercapnia with asphyxia, hypocapnia with diminished partial oxygen pressure in inhaled air, neuroemotional excitement during ascents in pressure chambers, physical load and dehydration when climbing mountains. At the same time, both hypercapnia [10, 11] and neuroemotional tension [12, 13], as well as physical loads [13, 14], could be in themselves the cause of increased production and excretion in urine of catecholamines.

In the opinion of a number of authors, the capacity to mobilize epinephrine reserves is very relevant to resistance to hypoxia [15, 16].

We have made an attempt to determine the link between elimination of epinephrine (E) and norepinephrine (NE) in urine in the presence of pressure-chamber

Table 1. Excretion of E and NE on days of ascent in pressure chamber (M±m)

TIME WHEN URINE SPECIMEN WAS TAKEN	E, μG/H					NE, μG/H				
	NORMAL	IA	IB	IIA	IIB	NORMAL	IA	IB	IIA	IIB
BEFORE TEST (0700-1000 HOURS)	0,44±0,1 n=9	0,61±0,4 n=27	0,51±0,2 n=9	0,54±0,1 n=3	0,63±0,3 n=9	0,82±0,2 n=8	1,07±0,7 n=29	1,35±0,6 n=10	0,92±0,3 n=3	0,93±0,6 n=8
DURING TEST (1000-1400 HOURS)	0,40±0,1 n=12	0,91±0,4 n=26	0,53±0,3 n=11	0,79±0,2 n=7	0,61±0,2 n=10	0,90±0,3 n=12	1,34±0,5 n=28	1,12±0,6 n=11	1,31±0,4 n=7	1,19±0,6 n=10
AFTER TEST (1400-1800)	0,50±0,2 n=8	0,60±0,4 n=29	0,41±0,2 n=8	0,35±0,2 n=4	0,53±0,2 n=7	0,73±0,3 n=10	1,14±0,7 n=29	1,03±0,8 n=9	0,87±0,6 n=4	1,00±0,3 n=7
1800-2300	0,33±0,2 n=5	0,44±0,2 n=28	0,44±0,3 n=9	0,25±0,1 n=3	0,39±0,2 n=8	0,78±0,3 n=4	1,06±0,3 n=25	0,89±0,4 n=8	0,71±0,3 n=3	0,81±0,4 n=8
2300-0700	0,17±0,01 n=5	0,24±0,1 n=26	0,17±0,1 n=8	0,16±0,1 n=4	0,26±0,1 n=7	0,53±0,2 n=5	0,57±0,2 n=25	0,51±0,2 n=9	0,49±0,2 n=4	0,63±0,4 n=6

hypoxia and intensity of the factor, as well as its tolerance, in the belief that this could make a contribution to determination of both the pathogenesis and physiological implications of the reactions in question.

Methods

We conducted this study on healthy young men 18-20 years of age, who were submitted to decompression in a pressure chamber. They all lived in the lowlands and were not adapted to hypoxia. In all, we used the hypoxic factor 88 times, and in the control group there were 22 analyses.

E and NE were assayed in urine acidulated to pH 3 with hydrochloric acid; the urine was stored in a frozen state until the day of the analysis. The results of control assays revealed that there was no loss of catecholamines in 2 months. E and NE were assayed by the trioxy indole method after isolation on aluminum oxide. For this purpose, the sample of E was acidulated with 0.25% potassium ferricyanide at pH 4.2 and NE with 0.5% potassium ferricyanide at pH 6.2. In the former case, the reaction was stoppped with 0.3% ascorbic acid solution and in the latter, with 0.5 M thioglycolic acid solution in 2.5 N NaOH containing 0.05 M formaldehyde. Fluorescence was measured with an Aminco-Bowman instrument, with excitation wavelength of 410 nm for E and 420 nm for NE; in both instances, fluorescence was measured at 520 nm. The method of separate measurement of E and NE was proposed by Andersson [17], and we used it in our modification.

We are combining here the results of five independent series of studies that were conducted at different times.

The first series involved a standard pressure-chamber test for 30 min at rarefaction corresponding to an

altitude of 5000 m. We tested 37 healthy young men who had not participated in such studies previously. They were tested in the mornings. Urine was collected at 3-5-h intervals around the clock (Table 1). The subjects were divided into two groups according to the sum of all physiological reactions: IA--with good tolerance and IB--with poor tolerance. A drastic drop of blood pressure was considered the chief physiological symptom determining poor tolerance of the pressure-chamber test.

In the second series, we determined the time reserve with rarefaction corresponding to altitudes of 6500-7000 m. In this series, only subjects who tolerated well the standard altitude chamber test were involved. The subjects were also divided into two groups. We determined simple reserve time with subjects in group IIA. Decompression was produced with the subjects breathing pure oxygen; then they were switched to air until there were marked signs of hypoxia, after which we again connected up the oxygen and effected the "descent." In group IIB, time reserve was examined similarly, but twice at 10-15-min intervals in the course of one decompression. Urine was collected in the same manner as in the first series.

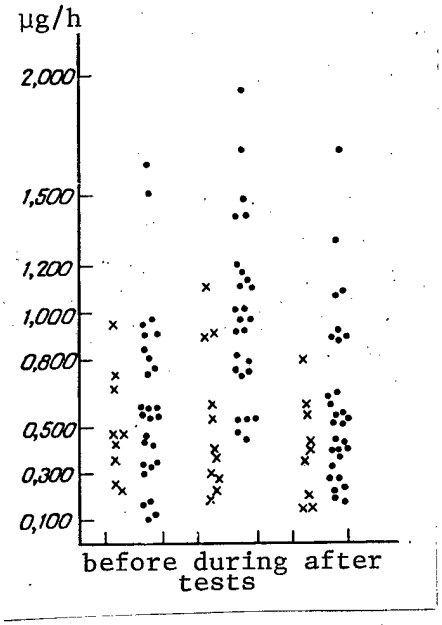
In the third series, the subjects spent 24 h in the pressure chamber at rarefaction corresponding to an altitude of 3500 m and in the fourth series, to an altitude of 4500 m.

In the fifth series, the conditions were the same as in the fourth, but every 2.5 hours the subjects breathed an oxygen-enriched mixture for 10 min. Only 24-h urine was analyzed in the third to fifth series.

Results and Discussion

In the daytime, excretion of E and NE is usually greater than at night, and many authors have paid attention to this; however, this parameter is usually the same in the morning and daytime [18]. During the standard pressure-chamber tests (first series) and determination of time reserve (second series), excretion of E in urine was higher in most cases than before or after the test. It was also above control levels (see Table 1). Mean levels of NE excretion in the same periods were higher in some cases during the test, but the differences were minor and unreliable.

In order to determine the cause of the adrenal reaction to acute hypoxia (shortage of oxygen or concomitant factors), we compared the results obtained for subjects in groups IA, IIA and IIB. Since the time reserve was determined only in subjects with good tolerance of the standard pressure-chamber test, we can consider the material studied to be homogeneous. We were also impressed by the fact that elimination of E during the test period was considerably higher in group IA than IIA and IIB, although in the latter case the rarefaction was greater. This could be attributed to the fact that E is secreted not only in response to hypoxia, but to neuroemotional stress, which was apparently greater in the subjects who had participated in the tests for the first time. In group IIB subjects, exposure to hypoxia was almost twice as long as IIA, but hourly excretion of E was even somewhat lower. We also failed to demonstrate a link between duration of hypoxia ("time reserve") and elimination of E (coefficient of correlation for overall duration of hypoxia was 0.16 and for the first exposure 0.123).



Effect of hypoxia on dynamics of E excretion

Dots and x's indicate groups of subjects who tolerated hypoxia well and poorly, respectively.

There was appreciably less excretion of E during the test period in group IB than in group IA, although duration of hypoxia was virtually the same. This reinforces the view [15, 16] that catecholamine reactions play a part in resistance to hypoxia. Some subjects, who tolerated the pressure-chamber test poorly, nevertheless excreted much E, whereas others, who tolerated it well excreted little E (see Figure). For this reason, we can only discuss tentatively the significance of capacity to mobilize adrenal reserves to endurance of hypoxia. It should also be mentioned that only absolutely healthy subjects participated in our tests, and they had undergone strict medical screening. It is quite probable that there will be many who excrete E but have poor tolerance for the pressure chamber test among individuals with lower health standards. A comparison of parameters for groups IA and IB leads us to assume that emotional adrenal reactions play a positive role in resistance to hypoxia.

Overall E and NE excreted in urine per day in the first and second series of tests (Table 2) were not very informative. On the average, there was slightly less elimination of NE than in the control.

Table 2.
Daily excretion of E and NE in urine after hypoxia (M±m)

SERIES OF STUDIES	n	E, µG	NE, µG
NORMAL LEVELS	22	8,12±2,35	27,7±8,51
I			
A	26	10,8±3,4	21,6±5,8
B	11	8,3±2,8	10,0±5,5
II	13	8,4±2,0	17,5±4,3
III	14	11,7±4,9	22,7±11,8
IV	13	14,2±4,0	24,0±6,2
V	11	12,4±4,5	23,8±2,0
A	5	10,6±3,7	19,8±3,1
B	6	13,4±5,3	27,2±4,0

Thus, one can best interpret the results of tests with acute hypoxia if we consider that output of E is not determined by hypoxia itself, but by concomitant neuro-emotional stress, but the adrenal reaction causes better endurance of the test.

In the third and fourth series of tests, in which the subjects spent 24 h at barometric pressure corresponding to 3500 and 4500 m, there was no reliable change in elimination of E and NE, as compared to control levels (see Table 2). Intermittent delivery of oxygen, which improved endurance considerably according to both subjective and objective physiological signs, did not affect excretion of E and NE in urine. Thus, hypoxia lasting 1 day, against a background of minimal physical activity and in the absence of strong emotional stimuli, was not associated with catecholamine reactions.

If we were to divide the subjects involved in the fifth series of tests into two groups (VA with headache VB without headache) on the basis of subjective complaints, we would find that VB group subjects excreted somewhat more catecholamines in urine (see Table 2). This could be attributed to the fact that weakening of functional capacity of the cardiovascular system was manifested by impairment of cerebral and renal circulation, because of which the subjects had a headache and excrete less substances in urine. This assumption is confirmed by the higher levels of diuresis in group VB subjects (average 1200 mℓ), whereas the average for group VA subjects was 900 mℓ/day.

Our findings can be compared to the data of Grover et al. [9], who conducted pressure-chamber experiments using a chemical method that was not too refined, and who were able to demonstrate that a 4-day stay by subjects in a pressure chamber at rarefaction of 440 mm Hg (which corresponds to an altitude of 4500 m) did not alter E and NE excretion. However, when the atmosphere in the pressure chamber was enriched with carbon dioxide (so that partial tension in alveolar air would remain unchanged--to normocapnic hypoxia), there was drastic increase in total E and NE excretion in urine. On the basis of considerably more material and using a more sophisticated chemical technique for assaying E and NE, we were able to confirm the first part of the study of Grover et al., to the effect that prolonged exposure to pressure-chamber hypoxia per se does not elicit catecholamine reactions. There was also confirmation of the finding [15, 16] that, in a number of instances, individuals with pronounced adrenal reactions tolerate the pressure-chamber test better. However, we must stipulate here that this applies only to people, in whom the standard pressure-chamber test was associated with strong emotional reactions--in our studies this refers to the first series of tests, in which individuals participated who had never before encountered such tests. The studies of Artamonov were conducted on pilots undergoing expert medical certification of fitness for flight work, so that there is no doubt that their emotional background was also rather pronounced. At the same time, our findings convince us that individuals who are accustomed to pressure-chamber tests can tolerate brief hypoxia well even if they present no marked adrenal reactions.

Thus, the overall data we obtained enables us to draw an unequivocal conclusion to the effect that pressure-chamber hypoxia (brief or lasting for 1 day), if not complicated by concomitant factors, does not cause increase in E or NE excretion in urine, although in some cases the adrenal reaction could be instrumental in better tolerance of hypoxia.

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INVESTIGATION OF PROCESS OF DECOMPOSITION OF WHEAT STRAW UNDER ARTIFICIAL CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 16 Nov 81) pp 75-79

[Article by Ye. A. Deshevaya, I. V. Kryuchkova, Yu. I. Shaydorov and V. V. Popov]

[English abstract from source] This paper presents the results of experimental studies of wheat straw degradation under artificial conditions. During the 28-day study dry matter losses were 26%. Dissolved organic substances were accumulated during the first 4 days and remained practically unaltered thereon. Minerals (except for potassium) were dissolved during the first 2 days. The degradation occurred with a distinct periodicity reaching maximum on days 2-4 and 14-16 and was associated with a change in the predominant microorganisms. The intensity of microbial development and carbon dioxide production during degradation was linearly correlated. The growth of coleoptiles was inhibited by wheat degradation products due to phenylcarbonic acid. As the degradation continued, the structure of dissolved organic substances became more complicated and the condensation of aromatic nuclei increased. This was indicated by a change in the optic density of solutions and the slope of spectral curves.

[Text] Waste processing in a biological life-support system (BLSS) must be adequate to corresponding processes in the biosphere and instrumental in creating a proper habitat for autotrophic and heterotrophic organisms [1-3].

The existing conception that minerals can furnish all that is necessary to a plant is fallacious [4-7]. It has been determined that a number of organic compounds, including products of bacterial decomposition of plant residue, have a beneficial effect on plants [8-18]. For this reason, it is necessary to investigate the principal patterns of decomposition and transformation processes in plant residue in order to determine the ways and means of using them as the sole processes in a closed ecological system in order to increase the extent to which it is closed with regard to mass exchange.

We shall discuss here the dynamic features of the process of straw decomposition over a long peirod of time, commensurate with the time of humus production.

Method

Summer wheat straw was cut into pieces 2-3 cm in length, placed in cylindrical columns (90 mm long, 300 mm tall) and covered with distilled water at the rate of 1 ℓ/70 g dry wheat mass (per column). The contents of the columns were aerated continuously with atmospheric air, outlay of which constituted 0.5 ℓ/min. The temperature of fluid in the columns was kept at 18-22°C. We did not inoculate the straw with any cultures of microorganisms. In the course of its decomposition, we made a dynamic study of the following parameters: decrease in amount of straw, by weighing all of the straw in each column when it was dry (brought to a constant mass); rate of output of carbon dioxide using an OA-2209 gas analyzer, according to its accumulation with air circulating in the closed system; composition and quantity of microflora: saprophytic bacteria on beef extract agar, yeast on wort agar, fungi on Czapek medium, actinomycetes on starch-ammonia agar and microorganisms that degrade cellulose on Hutchinson's medium as modified by Pushkinskaya [19]. The Koch method was used for inoculations [20]; isolation in solution of minerals--total nitrogen and phosphorus by colorimetry after ashing, K, Ca, Mg, Na by flame spectrometry; dry matter content of fluids and total organic matter by weighing the dry residue after desiccation of unadulterated and dialyzed fluids; absorption spectra using an SF-10 spectrophotometer and FEK-56M photocolorimeter; presence of growth regulators in solutions by a combined technique of demonstrating growth regulators, consisting of lyophilization of tested fluid, extraction of residue with ethyl ether, chromatographic separation of ether extract using one- and two-dimensional chromatography on paper in different systems of solvents. Chemical identification of the substances exposed on chromatograms was made on the basis of rf values, fluorescence in ultraviolet light, qualitative reactions to phenol compounds and ultraviolet spectra of absorption of the tested substances [21] evaluation of biological activity of fluids on radish seedlings and in coleoptile tests [22].

Results and Discussion

The decrement of dry matter of initial straw mass constituted 25.8% in 28 days. The rate of decomposition diminished in the course of the experiment from 1.7-1.8 g/day at the start of the experiment to 0.25 g/day on the 17th day, increasing to 0.9 g/day by the end of the experiment. Accumulation of organic matter in fluid, including biomass of microorganisms, was observed for the first 4 days of decomposition. Thereafter the content underwent virtually no change.

The levels of the main trace elements in the initial straw were as follows (in mg/g dry mass): N 4.60, P 0.92, K 10.20, Ca 2.95 and Mg 0.43. Discharge of the elements studied (with the exception of K) from straw and accumulation in fluid occurred primarily in the first 2-3 days of the experiment. In the course of subsequent decomposition of straw, there was insignificant change in amount of elements in solution and it constituted the following amounts (percentage of levels in original straw): N, P and Ca 15-20, Mg 50 and K from 55 at the start of decomposition to 90 at the end of the experiment.

Quantitative and qualitative assays of microorganisms (fungi, yeast, bacteria, actinomycetes, cellulose-degrading microorganisms) revealed two distinct periods of intensive development of microorganisms: the first from the 1st to 10th days and the second from the 8th-10th day to the end of the experiment (Figures 1 and 2). In the first period, we observed an increase in number of

yeast cells and cellulose-digesting microorganisms and at the end of the period, fungi. The quantity of bacteria that utilize organic forms of nitrogen gradually diminished by the 10th day after a brief increase on the 2d day. The prevailing microorganisms were saprophytic bacteria Bacillus, Pseudomonas, Lipomyces yeast, Penicillium Mucor fungi, cellulose-degrading Sorangium and Cytophaga microorganisms. The second period was characterized by considerable development of fungi, increase in quantity of yeast, saprophytic bacteria and cellulose-destroying microorganisms. Maximum quantities of fungi and yeast were demonstrable on the 14th day, maximum saprophytic bacteria utilizing organic forms of nitrogen were found on the 17th day of decomposition. From the 21st day, actinomycetes appeared in the solution. The prevalent microorganisms were saprophytic bacteria Bacillus, Pseudomonas, Alternaria, Penicillium, Dematium, Verticillium and Aspergillus fungi, Streptomyces actinomycetes, cellulose-degrading Cytophaga, Cellvibrio, Sorangium and Polyangium.

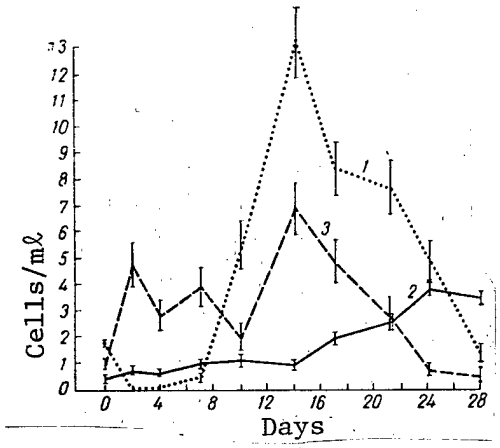

Figure 1.
Dynamics of microorganism populations in fluid during decomposition of straw
1) microscopic fungi ($\times 10^3$ cells)
2) cellulose-degrading microorganisms ($\times 10^4$ cells)
3) yeast ($\times 10^4$ cells)

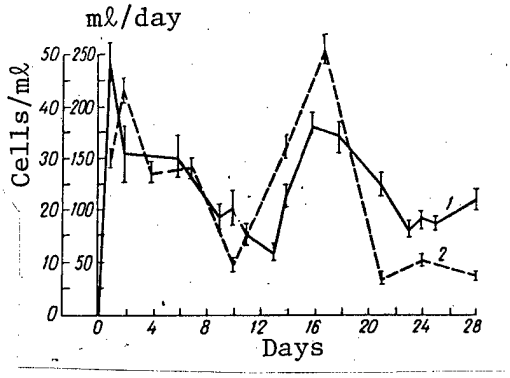

Figure 2.
Dynamics of carbon dioxide output and number of saprophytic bacteria during decomposition of straw
1) CO_2 output, mℓ/day
2) number of saprophytic bacterial cells per mℓ fluid ($\times 10^5$ cells)

The amount of carbon dioxide released characterizes the intensity of microbiological processes. Different researchers have reported both existence of a direct correlation between these processes and absence thereof [23-24]. In the experiments, we observed a coincidence of periods of intensive development of microflora and CO_2 output (see Figure 2).

Fluids recovered on the first 3 days of decomposition depressed coleoptile growth in a 1:5 dilution. At later stages, we did not observe inhibition of coleoptile growth by the fluid.

The chromatograms demonstrated two distinct spots with blue and yellow-green fluorescence in UV [ultraviolet] light. In 15% acetic acid, the spots were localized in the bottom part of the chromatogram (rf = 0.4-0.6) whereas in a mixture of butanol, acetic acid and water the rf of these spots constituted

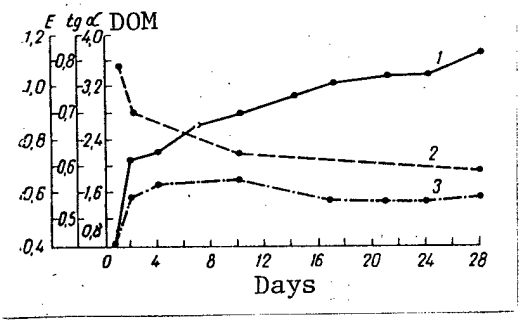

Figure 3.
Change in optical properties of fluid in the course of straw decomposition
1) optical density (E) at λ = 400 nm
2) tangent of angle of inclination of spectral curve (tan α)
3) sum of dissolved organic matter (DOM), g

0.5-0.7. Diazotized sulfanylic acid stained the spots a bright orange, whereas $FeCl+K_3Fe(CN)_6$ reagent colored them blue. Alcohol eluates of these spots presented the typical absorption spectra for phenol derivatives with maximum absorption in the region of 285 and 330 nm. According to all of the above features, the isolated substances were identified as phenolcarbonic acids. The maximum levels thereof in the fluid were demonstrated on the 3d day of decomposition of straw. On subsequent days, the color of the spots grew less intensive and there were mildly marked areas of maximum absorption. On the 8th day of decomposition, phenol compounds were not demonstrable in the fluid.

Fluids recovered on the first 8-10 days of decomposition in a dilution of 1:50 did not have an appreciable effect on seedling growth. Starting on the 10th day of decomposition, the fluids stimulated seedling growth by 30-40%.

The process of decomposition of plant residue is associated with humification [25-27]. One of the characteristics of products of plant residue decomposition, related to the process of de novo formation of humus acids, is their electronic absorption spectra. The inclination of spectral curves (slope of absorption spectra) is determined more or less to condensation of aromatic structures in molecules of humin acids. The most objective characteristic of the entire absorption spectrum in the visible region is the tangent of the angle of inclination of the line in coordinates log E - λ [28]. With increase in time of decomposition, the optical density of fluids and slope of absorption spectra increase, while the tangent of the angle of inclination of spectral curves diminishes (Figure 3).

The increase in optical density on the 1st experimental day could be related to increase in concentration of dissolved organic matter, as well as oxidation of clear phenol derivatives into strongly stained tannins [29]. The subsequent increase in optical density may be related to change in correlation between carbon contained in condensed aromatic nuclei that absorb light and carbon of side radicals which is transparent in the visible part of the spectrum [11]. The data indicate that, with increase in duration of straw decomposition, there is increase in share of aromatic structures and in amount of carbon in molecules of dissolved matter.

The results of this study indicate that the means of straw decomposition we have discussed can be used to recover biologically active substances--products of microbiological resynthesis, which are required for normal vital functions of plants in biological life-support systems. A method was developed and tested for processing plant residue into fertilizers, in order to further decompose straw by means of more complex destructive biocomplex on solid substrates [30].

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MATHEMATICAL MODELS OF SOME EXOBIOLOGICAL SITUATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 19 Apr 82) pp 79-81

[Article by V. V. Verigo and T. F. Ponomareva]

[English abstract from source] To analyze quarantine and sterilization requirements of spaceflights, the possibility of coexistence of terrestrial and aboriginal forms of life was theoretically explored. It was found that if the trophic chain with the terrestrial form acting as a consumer evolves both forms may coexist. Their quantitative relations can be explained by a good number of hypotheses. The study of spatial distribution and diffusion suggests wave-like processes similar to the distribution of autocatalytic reactions in chemical kinetics.

[Text] The question of existence of biological forms of matter beyond the limits of earth continues to be one of the most burning and relevant problems of modern cosmonautics. The research program implemented by U. S. specialists with Viking craft on the surface of Mars did not yield an unequivocal answer concerning the existence of life on Mars. While there have been some statements made by some scientists concerning the physicochemical origin of the effects observed [1], a different point of view also exists, whose proponents prove with rather good argumentation the possibility of biological interpretation of the same set of experimental facts [2].

Since this question has not yet been answered, all of the restrictions remain valid, with reference to sterilization and quarantine measures in practical cosmonautics [3]. For this reason, it is interesting to conduct a theoretical analysis of the possibility of coexistence of terrestrial and aboriginal forms of life if they come in contact. It is expedient to make a preliminary assessment of the efficacy and consequences of such global measures by means of mathematical modeling.

Let us consider the situation that arises in the event that an aboriginal biota adapted to living on a planet or products of its vital functions are a "suitable" source of nutrition for terrestrial organisms. If we assume that there are some elements in common in metabolic processes in the two forms of life, this variant appears to be more realistic than competition between them.

Without taking into consideration, for the time being, spatial effects, let us consider the concentration of terrestrial microorganisms a and concentration of aboriginal nutrient substrate c, changes in which in time can be described by ordinary differential equations in this case.

In our first analysis, it is also logical not to take into consideration the possible species diversity of a and c. Let us assume that, in the absence of extraplanetary influences, the limiting environmental factors determine an equiponderant value of c, a certain c^*. Let the rate of increment of c be proportional to the difference of $c^* - c(t)$ with a certain coefficient ϕ. The effect of a is additive and is manifested by consumption of c at a rate that is proportional to a. The intensity of uptake equals k. With regard to rate of change in a, let us assume that it is described by $\mu(c) - b$, where the rate of increment μ is related to presence of substrate c. In the absence of other information, it is permissible to assume that the function $\mu = \mu(c)$ has a Michaelis-Menten form [4]:

$$\mu = \mu_0 \frac{c}{\chi + c} \tag{1}$$

In this case, with low concentrations $c (c \ll \chi)$, the rate of increment of a is linearly related to presence of substrate. With high concentrations c $c \gg \chi$ its presence is no longer a limiting factor, the rate of reproduction of a is constant and equals μ_0.

In this formulation, we are not considering the autoinhibiting effects, and we assume that parameters ϕ, k, μ_0 and χ are constant. Under these conditions, the change in a and c as a function of time is defined by the system of equations:

$$\begin{aligned} \dot{a} &= \left(\mu_0 \frac{c}{\chi + c} - b\right) a \equiv P(a, c) \\ \dot{c} &= \varphi(c^* - c) - ka \equiv Q(a, c). \end{aligned} \tag{2}$$

System (2) has an obvious solution $a = 0$, $c = c^*$, $\dot{a} = \dot{c} = 0$ (3). Let us see if it is possible for there to be other stationary answers other than (3). The right terms of system (2) change to zero if:

$$\begin{aligned} a_0 &= \frac{\varphi}{k}\left(c^* - \frac{\chi b}{\mu_0 - b}\right). \\ c_0 &= \frac{\chi b}{\mu_0 - b}. \end{aligned} \tag{4}$$

Let us examine the stability of this stationary solution according to linear approximation by the usual methods [5]. The behavior of system (2) when there are minor deviations of a and c from (4) is defined by the characteristic equation:

$$\lambda^2 - \sigma\lambda + \Delta = 0, \tag{5}$$

the coefficients of which are linked to parameters of system (2) by the following relations:

$$\sigma = \left.\frac{\partial P}{\partial a}\right|_{\substack{a=a_0\\c=c_0}} + \left.\frac{\partial Q}{\partial c}\right|_{\substack{a=a_0\\c=c_0}}$$

$$\Delta = \left.\begin{vmatrix} \frac{\partial P}{\partial a} & \frac{\partial P}{\partial c} \\ \frac{\partial Q}{\partial a} & \frac{\partial Q}{\partial c} \end{vmatrix}\right|_{\substack{a=a_0\\c=c_0}} \tag{6}$$

In our case, $\sigma = -\varphi$

$$\Delta = \frac{\mu_0 \varphi c^*}{\chi}\left(1-\frac{b}{\mu_0}\right)\left(1-\frac{b}{\mu_0}\left(1+\frac{\chi}{c^*}\right)\right). \tag{7}$$

Let us consider the case where $\Delta>0$. Since it is relevant to consider only the situation in which $b<\mu_0$, this condition is satisfied with:

$$b<\frac{\mu_0 c^*}{c^*+\chi}, \text{ i.e., } b<\mu(c^*).$$

Since $\sigma<0$, the stationary solution is stable. Classification of a special point (a_0, c_0) depends on the sign of expression $\sigma^2 - 4\Delta$. With:

$$\varphi<4 \quad \mu_0 \frac{c^*}{\chi}\left(1-\frac{b}{\mu_0}\right)\left(1-\frac{b}{\mu(c^*)}\right)$$

the special point is a stable focus, otherwise it is a stable double point [node].

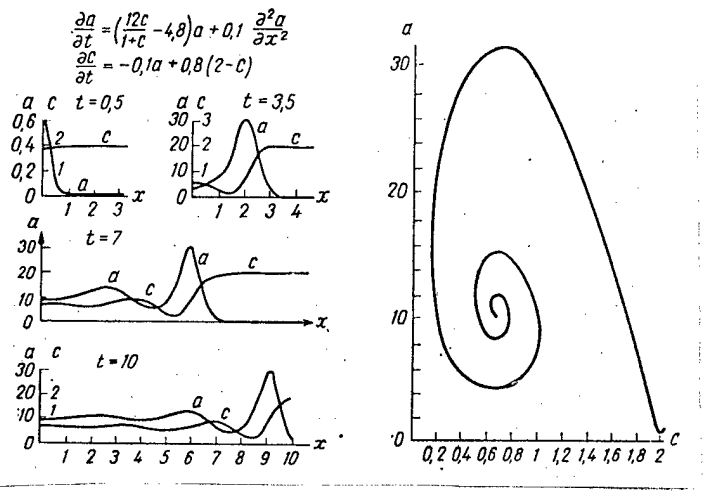
The case where $\Delta<0$ and the stationary solution corresponds to a special point of the saddle type is not realized if μ is a one-to-one function of c. Indeed, with $\Delta<0$, it is necessary for either inequality $\mu_0<\mu(c_0)<\mu(c^*)$ or $\mu_0>\mu(c_0)>\mu(c^*)$ to be satisfied. According to the meaning of formula (1), neither the first nor second inequality is possible, since $c_0<c^*$. Thus, with the base assumptions we have made, it is possible for two forms of life to coexist with stability. Let us note that this conclusion can also be derived from more general hypotheses for a system of the following appearance:

$$\begin{aligned} \dot{a} &= (f(c)-b)\,a \\ \dot{c} &= g(c)-ka \end{aligned} \tag{2'}$$

In this case, it is sufficient for the following conditions to be met:

$$\frac{\partial g}{\partial c}<0\ \frac{\partial f}{\partial c}>0.$$

which, according to the meaning of functions $f(c)$ and $g(c)$ appears to be quite plausible.



Example of dynamics of process of dissemination of a

Biological interpretation of these results consists of considering it possible for there to be stable coexistence of two forms of life, with realization of the above assumption concerning formation of a trophic chain with the terrestrial form as the consumer, with rather broad hypotheses concerning the quantitative characteristics of the structure of their interaction.

Consideration of spatial distribution and diffusion of a can be effected by means of analysis of the following system:

$$\frac{\partial a}{\partial t} = [f(c) - b]\,a + D\frac{\partial^2 a}{\partial x^2}$$

$$\frac{\partial c}{\partial t} = g(c) - k\bar{a}$$

There is a possibility of autowave [?] processes in the system, which are largely analogous to processes of dissemination of autocatalytic reactions in chemical kinetics [6].

The Figure illustrates the dynamics of processes of change in a and c for the initial uniform distribution of c and close to point "infection" of the environment by substance a at the start of the coordinates. We see that the phase diagram of the trajectories at the start of the coordinates corresponds to a stable point. One can also observe distribution of the "wave" of a as a function of time along coordinate x. In recent times, the problem of extending the markedly localized solution to a system described by a parabolic equation is being actively discussed in a number of works [7, 8].

Analysis of the problem we have discussed here is of great interest and presents considerable difficulties with regard to other variants of coexistence of a contaminating component of terrestiral origin and local form of life, in

particular, in the gas phase. However, investigation of more comprehensive formulations of the problem is related to the need for more detailed hypotheses concerning mode of existence and initial distribution of the aboriginal biota.

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CLINICAL STUDIES

UDC: 613.693-07:612.766.1

DETERMINATION AND CLINICAL ASSESSMENT OF PHYSICAL WORK CAPACITY OF FLIGHT PERSONNEL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 26 Jan 82) pp 82-84

[Article by V. M. Kondrakov, V. I. Koledenok and L. I. Arsen'yeva]

[English abstract from source] Using submaximal exercises, work capacity of 375 aircraft crewmembers, aged 20-49, was investigated. It declined slightly with age. The factors most frequently causing its decrease in healthy and diseased people were identified and methods of its measurement were refined. It was shown that the work load, chronotropic reserve index and cardiac index may give indirect evidence of the coronary blood flow rate, and the inotropic reserve index of the cardiac contractile function. Determination of work capacity of the flight personnel makes it possible to improve the medical supervision, detect at an early stage cardiovascular abnormalities and to substantiate expertise conclusions.

[Text] Physical work capacity (PWC) is an integral indicator of man's physical capacites in everyday life, professional work, physical culture and sports. PWC depends on morphological and functional condition of various systems of the body; however, the capabilities of the cardiorespiratory system are the chief factors [1-3]. From the PWC parameters, one can assess, not only qualitatively, but quantitatively, the functional state of oxygen transport systems, which is important to medical expert certification of flight personnel. Early forms of pathology of circulatory and respiratory organs are manifested primarily by a change in PWC parameters, which are compared to the age norms in such cases.

Our objective here was to investigate the nominal PWC levels and define some methodological aspects of their assessment.

Methods

A total of 375 flight personnel 20 to 49 years of age were tested at a hospital; they had been deemed healthy and admitted for flight work without restrictions. The subjects were divided into 3 groups: the first consisted of 132 people 20 to 29 years old (average age 26.1±1.31 years); the second

consisted of 158 subjects 30-39 years of age (average 34.6±1.26 years), and the third, 85 people 40-49 years of age (average 44.9±2.1 years).

As a load test for determining PWC parameters, we used physical exercise on a bicycle ergometer, with continuous increase in physical load, in steps, at submaximum force. In assessing the results of the tests, we took into consideration the level of performed exercise, heart rate (HR), blood pressure (BP) and electrocardiographic data. We calculated maximum oxygen uptake from the nomogram of Astrand-Ryhming [3], which was then related to unit of body weight. In addition, we calculated standardized relative ergometric parameters: index of chronotropic and inotropic reserve of the heart and index of myocardial tension.

Results and Discussion

The average energy of physical exercise constituted 984±15.4 kg-m/min for the first group and 990±14.9 kg-m/min for the second ($P<0.05$).* It decreased reliably in the third group, constituting 920±16.7 kg-m/min (P_1 and $P_2<0.001$). Performance of exercise at this level was indicative of functional integrity of the cardiorespiratory system, which is consistent with the results obtained by other authors [4, 5].

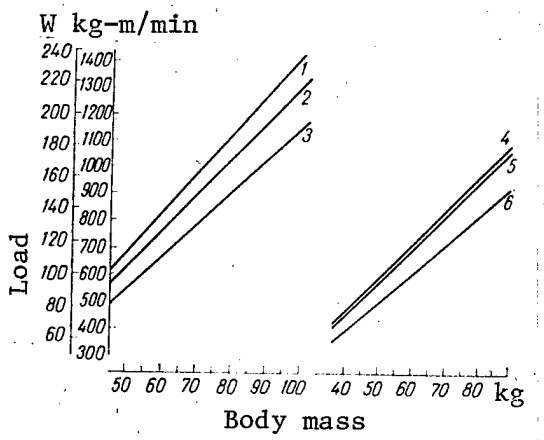
The cause of diminished energy could have been decrease in contractile function of the myocardium, respiratory insufficiency and deconditioning. In the presence of ischemic heart disease, coronary insufficiency is the chief limiting factor of work capacity [6]. These etiological factors must be taken into consideration when there is a decline in actual exercise energy, and one can determine the level of physical capacities of subjects from the degree of this decline.

Maximum oxygen uptake is the main indicator of efficient function of circulatory and respiratory organs. However, the direct method of its determination during physical exercise is difficult and not without danger. For this reason, maximum oxygen uptake was calculated indirectly from the above-mentioned nomogram. These values were related to the unit of body mass in order to compare the findings. Thus, oxygen uptake constituted 37.3±0.54 mℓ/min/kg in the first group of subjects, 36.6±0.51 mℓ/min/kg in the second and 35.4±0.66 mℓ/min/kg in the third. We demonstrated an insignificant but reliable decrease in oxygen uptake with age (P, P_1 and $P_2<0.001$). Studies have shown [7-9] that a decline of this parameter to less than 29 mℓ/min/kg is interpreted as an adverse reaction that leads to decline of PWC. This could be related to pathological changes in systems of oxygen transport or inadequate conditioning of the body. A low maximum oxygen uptake due to disease or hypodynamia can be corrected if exercises are included in the rehabilitation regimen.

The index of chronotropic reserve of the heart (ICR) is characterized by the ratio of HR increment at peak load to resting level, and it is expressed as a

*The following designations are used in this article: P--reliability of differences between parameters of 1st and 2d groups of subjects; P_1--the same, between 1st and 3d groups; P_2--same, between 2d and 3d groups.

percentage. It indirectly reflects productivity of the circulatory system as the principal factor in the oxygen transport system [2]. This is related to the the fact that, in most cases, HR during exercise is closely correlated with oxygen uptake, coronary blood flow and cardiac output. Mean ICR in the tested groups of subjects constituted 198.8±2.6, 191.0±2.3 and 185.9±3.7%, respectively (P, P_1 and P_2<0.001).



Submaximum load and approximate evaluation of bicycle ergometer test on subjects differing in sex, weight and age [10]
1-3) males, age groups 20-29, 30-39 and 40-49 years, respectively (HR 161, 156, and 152/ min)
4-6) females in the same age groups (HR 167, 160 and 154/min)

In the presence of sclerotic and inflammatory diseases of the myocardium, associated with damage to the sinus node, as well as after intake of β-adrenoblocking agents (obsidan, inderal), ICR declines. In a number of cases, even in well-conditioned individuals, the HR could lag behind the load level. It is imperative to take this into consideration when conducting bicycle ergometer tests, when the desire to reach a submaximum HR leads to artificial exaggeration of energy of performed exercises. Such mistakes can be avoided if submaximum loads are determined from the Shephard nomogram [10]] (see Figure). To do this, taking into consideration the sex and weight of the subject, from this nomogram, a vertical line was plotted to the intersection with the line for the corresponding age. A horizontal line is drawn from this point on the y-axis, showing submaximum force of the physical load.

A rise of ICR is encountered in patients with vegetovascular dystonia and some healthy individuals when they are deconditioned. In such cases, the HR is significantly ahead of the exercise load, while ICR does not reflect real productivity of the circulatory system. For this reason, when assessing this parameter it is necessary to take into consideration the physical exertion applied.

The increment of systolic BP during exercise as related to resting level, which is expressed as a percentage, is called the index of inotropic reserve (IIR). Its value is proportional to cardiac output, and for this reason it characterizes myocardial contractile function. According to our data, IIR was reliably dependent on the age of the subjects, constituting 171.0±2.8% in the first group, 166.2±2.2% in the second and 151.1±3.4% in the third (P, P_1 and P_2<0.001). An excessive increase in systolic BP and IIR during exercise is noted in individuals with neurocirculatory dystonia of the hypertensive type and grade I essential hypertension. A decline of IIR is encountered in the presence of myocardial pathology associated with impaired propulsive function of the heart.

The stress [tension] index (SI) is the product of HR multiplied by systolic BP. According to Robinson [11], the SI indirectly reflects oxygen uptake by the myocardium and, not infrequently, it is correlated with depression of the ST segment on the EKG. With a submaximum exercise load, as compared to resting

conditions, IS increased by an average of 287% in the first group, 283% in the second and 280% in the third. These high figures are an indirect indication of adequate coronary and myocardial reserves. A decline of this parameter is not uncommon in patients with coronary atherosclerosis, which reflects the inconsistency between myocardial oxygen requirement and capabilities of coronary blood flow. As a rule, such patients also present ischemic changes on the EKG during exercise tests.

Thus, the PWC parameters make it possible to assess more fully the functional reserves of the body, state of compensatory and adaptive mechanisms of the oxygen transport systems. One can assess the coronary reserve from the energy of performed exercise, ICR and SI, whereas the IIR permits evaluation of regulatory mechanisms of the circulatory system and myocardial reserve. In healthy individuals, a decline of these parameters is most often related to deconditioning, which means that a more active motor regimen and physical exercises should be prescribed for them.

Consequently, determination of individual levels of PWC parameters in individuals in flight professions would permit better dynamic observation of their physical condition, as well as detect early functional disturbances in the cardiovascular system, monitoring efficacy of health-improving and preventive measures, and validated back-up of an expert's decision.

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DEVICE FOR ACTIVE AND PASSIVE ORTHOSTATIC TESTS UNDER LABORATORY AND FIELD CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 22 Apr 82) pp 85-86

[Article by V. A. Dartsmeliya and G. S. Belkaniya]

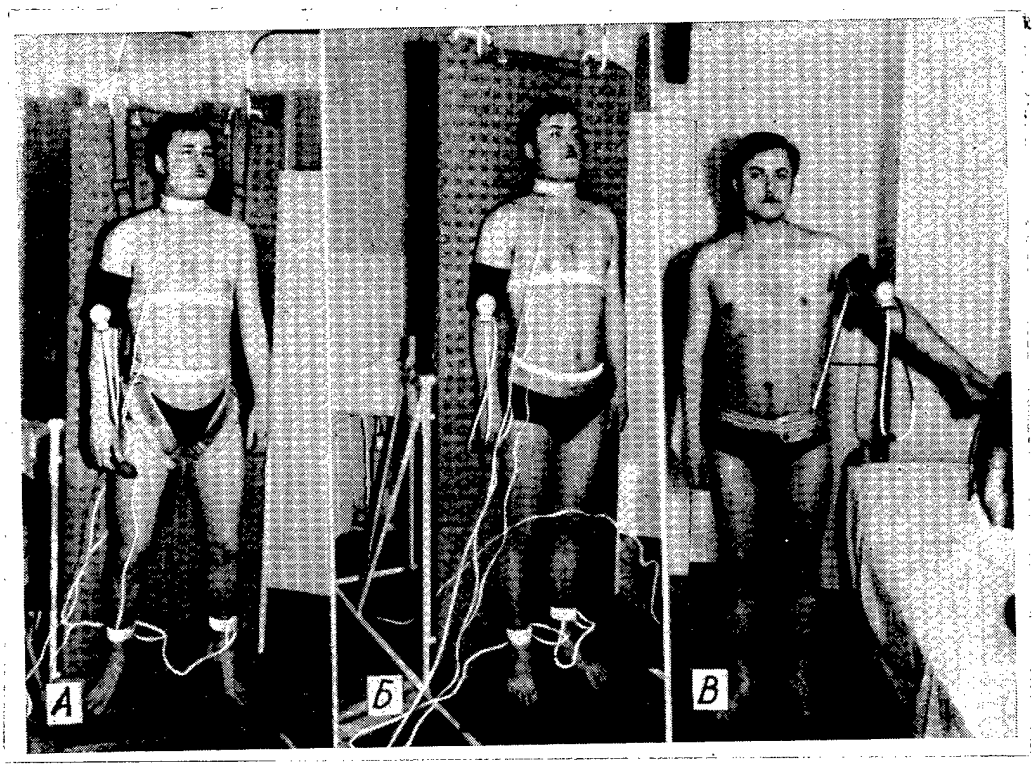
[Text] The active orthostatic test has been used for a long time in clinical practice for functional assessment of the cardiovascular system [1]. This test has gained particularly broad use in space medicine. This is related to the fact that orthostatic circulatory insufficiency is the most consistently demonstrable consequence of man's exposure to weightlessness or conditions simulating the physiological effects of weightlessness (clinostatic and anti-orthostatic [head tilted down] hypokinesia, immersion) [2].

Further expansion of studies with use of active and passive orthostatic tests is necessary to form an adequate base of facts to develop a conception of the standard range of functional characteristics of the body's main physiological systems in orthostatic conditions. For this reason, one of the important methodological aspects is to refine and standardize the equipment and methods used in such tests.

A turntable with saddle-shaped support is the traditional equipment for passive orthostatic tests. The small area of the support, high sensitivity of the perineum to pressure create some discomfort for the subject, especially when he has to remain in orthostatic position for a long time. The discomfort and instability of support on the saddle-shaped rest could be associated with involuntary muscular contractions, and they require use of additional immobilization of the trunk and upper extremities.

A system of immobilization on a turntable based on a parachute suspension (see Figure, A) was developed to overcome the above flaws in conducting passive orthostatic tests. The suspension consists of a system of straps with a lock device, which are distributed uniformly over the lower surface of the buttocks, internal and anterior surfaces of the thighs. The dorsal part of the strap system is attached to brackets on the head edge of the turntable and is the actual suspension part. For more uniform and convenient distribution of support, prevention of excessive tightness and compression of soft tissues of the thighs, prolon liners covered with fabric are secured to the support straps. Such a suspension system creates a rather stable position and comfortable

conditions for the subject to spend a long time in passive orthostatic position, and it does not require the use of additoinal immobilization devices.



Subject in passive orthostatic position with immobilization system made up of a parachute suspension (A), in active orthostatic position on the support platform of the turntable (Б) and during active orthostatic test under field conditions with use of support device to immobilize the hands (B)

Because the suspension system can be dismounted, it was possible to use the same turntable for active orthostatic tests. As we know, the conventional method for this test consists of having the subject independently move from supine to erect position. This move is associated with physical tension that is difficult to grade and consider, and this could have a substantial effect on parameters of hemodynamics, respiration and energy metabolism in the first few minutes after changing to erect position. Moreover, the difficulties could increase when there are various sensors on the subject's body, such

as electrodes to record the EKG, rheogram and other parameters. In turn, active change to erect position could cause interference and disturbances in the wiring system for recording functional parameters, which would make it difficult to conduct the test both with respect to schedule and planned program. To avoid all these problems, it is expedient to standardize the conditions for active orthostatic tests. For this purpose, a support platform was attached to the foot end of the turntable. The subject is placed in horizontal position, supine, in such a manner that the soles of his feet are in contact with the support platform. Changing to erect position is done passively by the researcher, whereas all active elements of stance are retained (see Figure, Б).

Thus, the removal immobilization device made from a parachute suspension and foot platform make it possible to use the turntable of this design for both active and passive orthostatic tests under laboratory conditions.

The greatest problems in conducting active orthostatic tests in the polyclinic or field arise when measuring blood pressure on a poorly immobilized arm of the subject. We developed a support, consisting of an immobilization belt, which is put on the thigh, a light bracket (formed metal plate, through which the strap is passed) and a movable shoulder support. This entire light support system makes it possible to immobilize the subject's arm in a stable position in order to avoid undesirable muscular tension, as well as to measure blood pressure under standard conditions (see Figure, B).

The above equipment should help standardize the method and conditions for active and passive orthostatic tests under laboratory and polyclinic (field) conditions.

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EFFECT OF PROLONGED HYPOKINESIA ON MINERALIZATION OF HUMAN CALCANEUS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 8 Apr 82) pp 86-88

[Article by Yu. Yu. Osipov and V. S. Shashkov]

[Text] The problem of demineralization of bones in weightlessness and with restricted motor activity continues to draw much attention on the part of researchers. In some works [1-3], the submitted data are indicative of appreciable decrease in bone mineralization, whereas demineralization is not noted in others [4-5]. There are publications [6-8], in which contradictory findings are reported.

Most researchers do not question the fact that osteoporosis develops during spaceflights or under hypokinetic conditions; however, our conceptions on this score are not exhaustive enough as yet to characterize the mechanism of the developing changes in mineral metabolism, or to assess the magnitude and duration of calcium loss, and to formulate with sufficient validation the measures for prevention and correction of existing deviations during the period of man's adaptation to weightlessness and after it.

Our objective here was to investigate the effect of long-term hypokinesia and various physical exercises on mineralization of the human os calcis.

Methods

This study was conducted with the participation of 18 healthy men 32-37 years of age, who were divided into three equal groups. The first group consisted of subjects who spent 182 days under antiorthostatic (-4° head tilt) hypokinetic conditions (control); the second consisted of subjects who performed physical exercises (for 2 h/day with energy expenditure of 300 kcal/h) under hypokinetic conditions and were submitted to myoelectrostimulation, and just prior to termination of bed rest they were conditioned with use of LBNP [lower body negative pressure] and fluid-salt supplements. The (full) set of exercises performed by the second group of subjects included pedaling on a bicycle ergometer, academic [?] and popular styles of rowing, walking, running and leaps in supine position (for 1 h in the morning and evening). Overall energy expenditure constituted 600 kcal.

The abbreviated set of exercises performed by the third group of subjects consisted of periodic exercise with an expander and pedaling on a bicycle

ergometer in supine position. Duration of exercises and energy expenditure did not exceed 30-50% of what the second group performed.

According to current conceptions, when negatively charged mu-mesons (muons) stop in the substance of a tested specimen there is release of the spectrum of meso-x-radiation that is typical for a given chemical element. If there are several elements in the specimen, several spectra appear. Analysis of the energy spectrum of a specimen makes it possible to determine the quantity of atoms in mechanical mixture from the intensity of groups of lines inherent in different atoms. The probability of a mu-meson stopping on different atoms of chemical compounds depends not only on the relative content thereof, but nature of chemical bond and atomic mass of the element. Since the patterns of mu-meson stops in complex chemical compounds have not yet been established in a general form, it is impossible for the time being to make an absolute element analysis of unknown compounds by examining only the meso-x-ray spectrum. However, if we assume that the nature of chemical bonds and atomic mass of calcium and phosphorus are constant in human bones, it is deemed valid to use this method for the purposes of this study. Unlike densitometry of x-rays, photon absorptiometry and x-ray tomography, which have been used in a number of studies, the method based on analysis of meso-x-radiation enables us to examine the dynamic levels of different elements in a living organism, and with a rather negligible radiation load.

Mineralization of bone was measured in the central segment of the left calcaneus before and 4 days after 182-day hypokinesia. This segment was identified by means of preliminary "soft" x-rays of the foot and its external anatomical reference points. The subject's food was immobilized in a support to rule out inclusion of other tissues of the foot in the muon beam, and the beam diameter was limited to 28 mm. The detector of meso-x-radiation was placed directly under the heel. Time of exposure to muons constituted 3 h. Radiation dose to the body as a whole and to the leg constituted 0.07 and 0.3 rem, respectively. The spectrum of meso-x-radiation was measured with a diagnostic muon beam of the synchrocyclotron at the Laboratory of Nuclear Problems, Joint Institute of Nuclear Research. Calcium and phosphorus levels in bone were interpreted as relative intensity of meso-x-radiation of the corresponding atoms. Mineralization of bone was used to refer to the sum of "relative contributions" of calcium and phosphorus. In view of technical problems, background data were not obtained for 3 people from the second and third groups. In this case, a comparison of the results was made using an average value for all background studies. The data were submitted to processing by variance and correlation analysis.

Results and Discussion

According to the data listed in Table 1, mineral content of the os calcis increased by 24 and 31% in 2 subjects of the first group, as compared to base levels. However, in the group as a whole, mineralization diminished and constituted 80.7% of the base levels after 182 days of hypokinesia. An analogous decline (by an average of 16%) was also observed in the case of combining hypokinesia with a full set of preventive measures. As can be seen from the data in Table 1, this change was not the same, and in 1 subject mineralization of the bone increased by 18%. The changes in the third group of subjects were

considerably more homogeneous. In this group, the change in mineralization constituted 12.5% of the base levels. There were no instances of increase in minerals. By virtue of the considerable variability of the data, the statistical relevance of changes in subjects of the second group was insignificant, and in the other two was in the nature of a tendency ($P<0.1$). Mineral content of the bone constituted an average of 5.6±0.33 and 4.7±0.19% in all subjects, before and after the study, respectively.

Table 1.
Mineralization of bone (Ca and P, % of elements demonstrable in meso-x-ray spectrum)

Group of subjects	Mineralization	
	before hypokinesia	after hypokines.
1	8,0	3,9
	5,0	5,8
	3,8	5,0
	5,5	4,2
	6,8	3,8
	5,0	5,0
	(5,7±0,59)	(4,6±0,34)*
2	4,0	3,5
	5,4	6,4
	6,1	6,0
	—	3,8
	—	4,6
	—	3,8
	(5,2±0,54)	(4,7±0,49)
3	6,1	4,7
	5,7	5,0
	5,8	5,1
	—	5,7
	—	4,5
	—	4,5
	(5,9±0,18)	(4,9±0,22)*
	(5,6±0,33)	(4,7±0,19)**

Note: Here and in Table 2, M±m for groups and in the bottom line for all subjects.
*$P<0.1$ **$P<0.05$

Table 2.
Ca/P ratio in bone tissue

Group of subjects	Ca/P	
	before hypokinesia	after hypokines.
1	2,1	3,3
	2,3	2,9
	3,2	3,2
	2,4	2,8
	3,5	1,9
	4,0	1,4
	2,9±0,33	2,6±0,35
2	3,0	2,9
	2,9	2,8
	4,5	2,8
	—	2,5
	—	2,5
	—	1,9
	3,5±0,46	2,6±0,16*
3	2,8	3,3
	3,8	3,1
	2,9	2,4
	—	2,8
	—	2,5
	—	3,5
	3,2±0,22	2,9±0,23
	3,1±0,22	2,7±0,14

A comparison of base and end levels of mineralization shows that it changed reliable in the direction of decrease under the effect of a factor in common for all subjects (in this case, hypokinesia). In assessing the described changes in composition of bone, it is interesting to note that, according to some data, mineral content of os calcis was in the range of 68-100% of the base level after 20 weeks of hypokinesia.

Mineralization of bone in subjects who performed a complete and abbreviated set of physical exercises for preventive purposes during the period of hypokinesia constituted 4.7±0.49 and 4.9±0.22%. In the group of subjects who took no preventive measures, mineralization was 4.6±0.34%. Consequently, these results do not enable us to state that either the full or abbreviated set of preventive measures had a beneficial effect. According to the results of other studies [9], exercises also failed to prevent demineralization of bone under hypokinetic conditions.

The method we used here enabled us to assess separately the changes in Ca and P constituents of bone minerals. As shown in Table 2, tendency toward decline of Ca/P ratio was inherent in most subjects after hypokinesia. Apparently, this could be indicative of the fact that predominantly Ca metabolism is involved in the osteoporosis process.

When we analyze individual data, we can see that changes in bone mineralization are the most marked in individuals with extreme values. Correlation analysis revealed (r = -0.61) a reliable ($P<0.05$) negative relationship between initial mineralization and the end level. An analogous correlation was observed in the crew of the Skylab orbital station after spaceflights [10].

Thus, our data are indicative of some decline in mineralization of the human os calcis and inefficacy of the sets of physical exercises used as a preventive measure on subjects who spent 182 days under hypokinetic conditions. However, the presence of a reliable correlation between severity of osteoporosis and initial bone mineralization does not enable us to consider demineralization as an absolute attribute of these studies. If such a correlation is confirmed in other studies, the question will arise as to including an analogous type of test in the program of clinical and physiological examination for purposes of cosmonaut screening. In this case, the method we used here may turn out to be not only promising, but the only possible one.

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BRIEF REPORTS

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CATECHOLAMINE CONTENT OF ISOLATED RAT HYPOTHALAMUS NUCLEI AFTER FLIGHT ABOARD COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 17 Aug 81) pp 89-90

[Article by R. Kvetnansky, Yu. Chulman and R. A. Tigranyan (CSSR, USSR)]

[Text] The hypothalamus, which is the main mediator between the central nervous (CNS) and endocrine systems, is richly innervated with catecholaminergic fibers, and it contains relatively large amounts of noradrenalinergic, dopaminergic and adrenalinergic fibers [1]. The presence of catecholamines (CA) in the rat hypothalamus, as well as their exact localization in its nuclei, has been recently demonstrated by means of precise biochemical techniques [2-4]. One of the important functions of CA in the hypothalamus is their participation in regulating liberin or hormone secretion and, consequently, in regulating the function of virtually the entire endocrine system [5-7].

Long-term spaceflights are associated with numerous factors that affect neuroendocrine reactions and, on this basis, it can be assumed that there are changes in CA metabolism in the hypothalamus under the influence of spaceflights. However, the studies we conducted in experiments aboard Cosmos-782 and Cosmos-936 biosatellites [8, 9] failed to demonstrate changes in CA concentration, activity of enzymes of their synthesis (tyrosine hydroxylase and dopamine-β-hydroxylase) or degradation (monoamine oxidase) in the whole rat hypothalamus under the effect of prolonged spaceflights.

Considering the current data on multiple functions of the hypothalamus, investigation of CA metabolism in the whole hypothalamus is less valuable. In recent years, many remarkable results have been obtained with the method of isolating individual nuclei from the hypothalamus and other structures of the brain [10]. All this prompted us to conduct a study of CA levels in different hypothalamic nuclei in an experiment aboard Cosmos-1129 biosatellite.

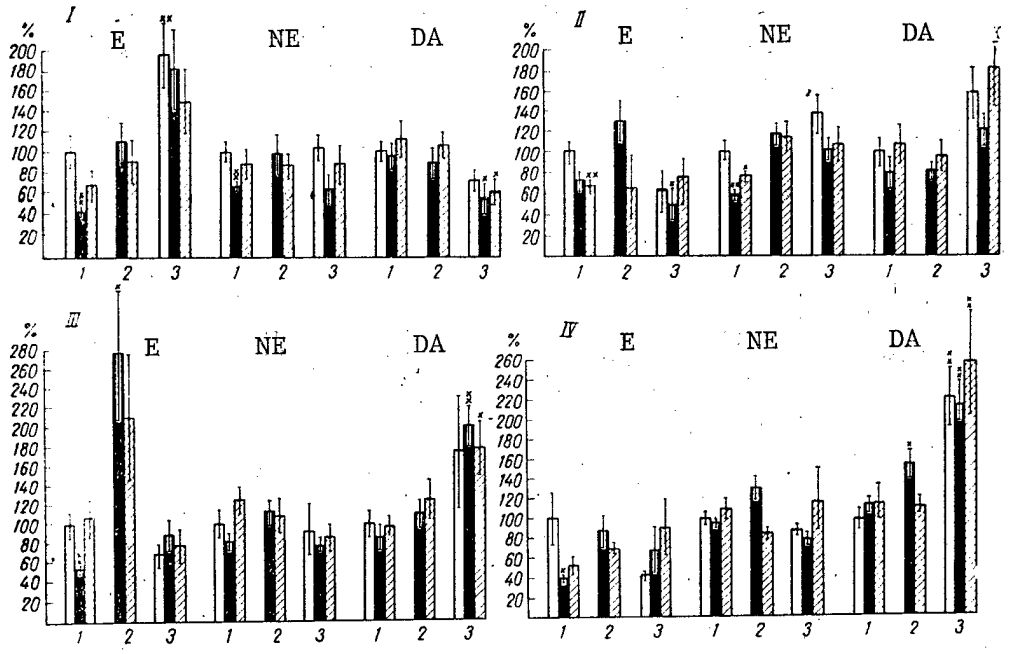
Methods

Studies were conducted with male Wistar SPF (Bratislava, CSSR) rats flown for 18.5 days in space aboard Cosmos-1129. The animals were decapitated 6-8 h and on the 6th day after the flight, and some of them, which were sacrificed on the 6th postflight day, had been submitted to immobilization stress 5 times (150 min per day). The rats in the control and synchronous experiment groups were also submitted to repeated immobilization stress.

Eight nuclei were isolated from the hypothalamus, which contained mainly nerve endings of monoaminergic neurons [10]. We assayed concentrations of epinephrine (E), norepinephrine (NE) and dopamine (DA) in nuclei by the radioenzymatic method [11, 12].

Results and Discussion

We observed a decrease in E and NE concentrations in the eminentia medialis of flight animals decapitated the moment they landed; in vivarium control animals, which were submitted to repeated immobilization, E concentration increased, whereas in flight rats and animals used in the synchronous control, DA dropped after repeated stress (see Figure, I). There was a decline in NE content of the nucleus arcuatus of flight animals immediately after landing, as well as in the corresponding synchronous control group. E concentration diminished in animals in the synchronous experiment group immediately after its conclusion and in flight rats submitted to repeated stress. DA concentration was increased only in animals of the synchronous group submitted to repeated immobilization (see Figure, II).



CA content (% of control) in eminentia medialis (I), nucleus arcuatus (II), nucleus periventricularis (III) and nucleus suprachiasmaticus (IV). Mean data (M±m) for 6-7 animals are illustrated. White columns refer to control, black to flight and stripped to synchronous experiment. One and two x's show $P<0.05$ and $P<0.01$, in comparison to intact animals.

1) immediately after landing
2) 6 days after landing
3) 6 days after landing + immobilization

Control (ng/mg):

I) 1.38±0.22 for E, 34.46±3.51 NE, 74.47±8.01 DA

II) 1.12±0.15 E, 37.2±3.35 NE, 27.4±3.51 DA

III) 0.50±0.07 E, 38.19±5.34 NE, 7.69±7.07 DA

IV) 0.50±0.13 E, 20.53±1.33 NE, 3.84±0.41 DA

E content in the nucleus periventricularis diminished in the flight group of rats who were decapitated right after landing. There was an increase in E concentration in rats sacrificed 6 days after landing, as well as in DA in flight and synchronous groups of animals submitted to repeated immobilization (see Figure, III).

In the nucleus suprachiasmaticus, there was a decrease in E concentration in the flight group of animals sacrificed immediately after landing, NE content did not change, while DA increased, as compared to the intact control, in flight animals on the 6th postlanding day in all groups submitted to repeated immobilization (see Figure, IV).

No changes in CA levels were demonstrable in the nucleus dorsomedialis and nucleus supraopticus of animals in all tested groups. E and NE content of the nucleus ventromedialis did not change in any of the groups. NE content in rats of the flight and synchronous groups submitted to repeated stress diminished, as compared to both the intact control and vivarium control animals submitted to repeated immobilization. Concentration of E and NE in the nucleus periventricularis of flight and synchronous groups submitted to repeated stress diminished, as compared to parameters for both intact animals and the vivarium control group submitted to repeated immobilization.

These results indicate that there are only a few regions of the hypothalamus that react, in the form of change in CA level, after a spaceflight, mainly the nucleus arcuatus suprachiasmaticus and perventricularis, as well as eminentia medialis, in which maximum changes had been previously demonstrated in CA levels following acute stress [3, 13, 14]. The low E and NE levels in these hypothalamic nuclei is convincing proof of the fact that the rats were under stress at the moment of landing. But was this acute or chronic stress? According to our results, which were obtained for rats submitted to repeated immobilization [3, 13, 14], in animals adapted in this manner there is an increase, rather than decrease, in CA levels in hypothalamic nuclei. On this basis, it can be assumed that the animals had not been submitted to chronic stress during spaceflight, since there was mainly a decrease in CA content in the hypothalamic nuclei. Most probably, the cause was acute stress that appeared during landing of the biosatellite.

In conclusion, it should be noted that we have yet to determine the significance of high CA levels in rats submitted to repeated stress. The question of whether this is beneficial or harmful also remains open.

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EFFECT OF ACETAZOLAMIDE ON CATECHOLAMINE EXCRETION IN THE PRESENCE OF ALTITUDE HYPOXIA (4.5 KM)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 19 Oct 81) pp 91-92

[Article by I. P. Yakovleva, I. S. Balakhovskiy, V. B. Malkin and N. F. Landukhova]

[Text] The question of the role of catecholamine reactions in endurance of oxygen deficiency has long since been on the agenda, since the answer to it would disclose some prospects of developing antihypoxia therapy. It is known that extreme degrees of hypoxia in animals cause release of epinephrine (E) and norepinephrine (NE) into blood [1, 2]. However, it is not clear what role is played here by hypoxia itself and the inevitable concomitant disturbances in acid-base equilibrium. Studies conducted during ascents in the mountains also do not always yield unequivocal results, since the body is exposed to an entire set of factors, the different elements of which are difficult to discern [3-5].

Some interesting studies have been conducted to determine the effect of hypercapnia on catecholamine (CA) excretion [6-9]. Thus, Grover et al. [8] investigated excretion in urine of E and NE together in two series of studies each lasting 5 days. These studies were conducted in a pressure chamber. In one of them, the subjects were submitted to rarefaction of 440 mm Hg (which corresponds to an altitude of 4500 m) and in the other, an analogous atmopshere was produced in the pressure chamber in such a way that partial oxygen pressure in inhaled air would be the same as in the first study, but because of addition of carbon dioxide its partial tension in alveolar air remained normal. In other words, a comparison was made of the effect of hypocapnic and normocapnic hypoxia. It was found that overall excretion of E and NE increased drastically only in the latter case. It was interesting to verify this finding in a study, in which the hypocapnic effect of hypoxia was attenuated in a manner different from breathing with mixtures rich in carbon dioxide. Such a possibility is provided by intake of acetazolamide (diacarb). This pharmacological agent is capable of inhibiting the enzyme, carbonate dehydratase (carboanhydrase), so that carbon dioxide is retained, and this causes less manifestation of hypocapnia and related disturbances of acid-base equilibrium.

Methods

This study was conducted with the participation of 12 healthy young men who spent 20 h in a pressure chamber at atmospheric pressure corresponding to an altitude of 4.5 km. Each subject was submitted to hypoxia twice, one with intake of diacarb and once with placebo. The subjects took diacarb in a dosage of 0.75 g/day for 3 days, and went into the chamber on the 3d day.

We collected urine during the day before going into the pressure chamber and the day of exposure to hypoxia, and assayed E and NE levels in it using a modification of the trioxyindole method.

Results and Discussion

The subjects complained of headache, respiratory disorder, nausea, sleep impairment and other well-known signs of mountain sickness during the time they spent in the chamber at an "altitude" of 4.5 km. Intake of diacarb provided considerable relief.

The Table lists excretion of E and NE in urine. As it shows, diacarb did not have a marked effect on CA excretion. Thus, in this instance, its beneficial clinical effect was not related to change in functional level of the adrenosympathetic system, but most probably to improved fluid-electrolyte balance.

Total excretion of E and NE during 20-h stay in pressure chamber at rarefaction (X±S, n = 12) corresponding to an altitude of 4.5 km above sea level

Excretion	Placebo intake	Diacarb intake
E, μg: without hypoxia	10.2±0.46	9.9±0.87
with hypoxia	14.2±1.26	10.7±1.30
NE, μg: without hypoxia	22.6±1.51	22.1±1.15
with hypoxia	24.0±1.85	20.8±3.00

Unlike the parameters obtained by Grover, there was no statistically reliable change in elimination of E and NE in our studies. There was even a tendency toward diminished excretion of E. Nor did hypoxia, either by itself or with intake of diacarb, have a reliable effect of CA production.

It is known that impairment of acid-base equilibrium could be the cause of marked increase in CA production [10]. It has been proven that respiratory acidosis plays some part [10, 11], but administration of soda to animals also elicited such a reaction, although in this case the changes were characterized as alkalosis [12]. Under hypoxic conditions, respiratory alkalosis caused by hypocapnia is compensated by metabolic acidosis, elicited by accumulation of insufficiently oxidized products, primarily lactic acid [13, 14]. It has been demonstrated [17] that respiratory compensation, i.e., increase in pulmonary ventilation leading to loss of CO_2 starts when 5 mmol/ℓ lactic acid accumulates in blood. Hence, it can be concluded that when human blood contains more than 4 mmol/ℓ (36 mg%) lactic acid, partial carbon dioxide pressure should drop,

otherwise there is development of such a degree of combined acidosis that physiological systems of the body must react. It is difficult to say whether such a phenomenon had been observed in the experiments [8], since blood composition was not analyzed. However, it can be assumed that the adrenal reaction was attributable more to acidotic changes elicited by increase in lactic acid content against the background of breathing gas mixtures enriched with CO_2, than to the influence of hypoxia.

Thus, neither the effect of hypoxia itself for a day, nor its complications due to inhibited activity of carboanhydrase elicits an increase in CA output.

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EFFECT OF PHARMACOLOGICAL AGENTS ON FLUID-ELECTROLYTE METABOLISM AND HUMAN RENAL FUNCTION DURING ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 28 Dec 81) pp 92-93

[Article by V. B. Noskov and V. V. Sabayev]

[Text] At the present time it has been demonstrated that it is theoretically possible to correct pharmacologically the adverse effect of weightlessness, as well as factors that simulate it (immersion, clinostatic and antiorthostatic [head-down] hypokinesia), on man [1-3]. In view of the necessity of implementing preventive measures at the earliest stages of spaceflights, questions of pharmacological support of spacecraft crews are becoming particularly timely. This study is part of investigations that address themselves to the search for pharmacological preventive agents, and it deals with assessment of effects of drugs referable to different groups of chemical compounds and combinations thereof on fluid-electrolyte metabolism and renal function in healthy man, since typical changes develop in fluid and electrolyte metabolsim in weightlessness and with factors that simulate its effects [4, 5].

Methods

Six healthy male volunteer subjects, 30-40 years of age, participated in this study; they spent 6 h in antiorthostatic (head tilted down at a -15° angle) hypokinesia (AOH). In all, there were 11 series of tests, and all of the subjects participated in each of them. In one series, we used "pure" AOH, i.e., the subjects did not take any pharmacological agent. The efficacy of drugs was assessed by the double blind method in comparison to placebo (lactose) (control hypokinesia). In the other series, some pharmacological agent or combinations of agents were used. There was an interval of at least 7 days between the different AOH series.

The subjects took the following agents by mouth 30 min before being put in antiorthostatic position: cholinolytic--scopolamine 0.0006; adrenomimetic and psychostimulant--ephedrine 0.025; agents with mediator and metabolic action--levopa 0.5, eskuzan 40 drops, stugeron 0.05. We also used combinations of scopolamine and levopa or ephedrine and stugeron with levopa or eskuzan. In these cases, the above-indicated dosage was also used.

All of the series of studies were conducted against a background of standard food allowance and monitored fluid intake, which enabled us to assess fluid balance during the AOH period. The subjects were weighed to keep a record of extrarenal fluid loss. We collected 24-h urine on the day of the study and different batches during AOH. Blood was taken from a vein before, during and after AOH. We assayed sodium and potassium in the collected specimens of blood serum and urine by the method of flame photometry (Jaffe reaction) and urea (according to reaction with paradimethyl aminobenzaldehyde). The results were submitted to processing by methods of variation statistics.

Results and Discussion

All of the agents used and combinations thereof had some beneficial preventive effect, i.e., most subjects reported improved well-being and endurance of AOH, as compared to control hypokinesia. According to subjective accounts, stugeron elicited a maximum effect.

The Table lists data on rate of excretion in urine of fluid and main electrolytes during AOH. As we see, when the subjects took placebo the tested parameters did not differ from data obtained with "pure" hypokinesia. Minute diuresis with intake of various agents and combinations changed insignificantly, and it did not differ appreciably from control levels--1.50±0.1 mℓ/min. A negative fluid balance in the range of 240 to 530 mℓ always developed during AOH. Weight loss constituted an average of 0.8±0.2 kg during 6 h of AOH. The agents taken did not have an appreciable effect on these parameters.

Rate of excretion of fluid, electrolytes, creatinine and fluid balance during AOH after intake of various pharmacological agents and combinations (M±m)

PHARMACOLOGICAL AGENT	DIURESIS mℓ/MIN	Na	K	Na/K COEFFICIENT	CREATININE, MG/MIN
		μEQ/MIN			
"PURE" AOH	1,8±0,2	281±29	58±7	4,7±0,6	1,60±0,30
PLACEBO	1,5±0,1	227±19	56±4	3,6±0,3	1,67±0,08
SCOPOLAMINE	1,7±0,2	216±28	21±7*	11,9±2,1*	1,56±0,14
EPHEDRINE	1,2±0,2	196±34	14±3*	14,2±4,4*	1,35±0,02
ESKUZAN	1,4±0,1	148±13*	21±1*	7,3±1,1*	1,44±0,3
STUGERON	1,9±0,3	236±31	46±7	4,6±0,4	1,46±0,14
LEVOPA	1,4±0,2	204±13	68±24	3,0±0,4	1,91±0,67
SCOPOLAMINE+EPHEDRINE	1,7±0,5	137±17*	50±8	2,9±0,4	1,50±0,11
SCOPOLAMINE+LEVOPA	1,9±0,6	266±46	59±10	4,6±0,3	2,27±0,3*
STUGERON+LEVOPA	1,4±0,2	222±11	69±6	3,3±0,3	1,72±0,12
STUGERON+ESKUZAN	1,7±0,1	192±14	41±5*	4,8±0,3	1,43±0,12

*Reliable differences ($P<0.05$) as compared to control (placebo intake).

Since blood serum creatinine concentration changed insignificantly in all subjects and in virtually all series of tests, remaining within a range that was close to the physiological norm, the rate of creatinine excretion in urine corresponded to glomerular filtration. There was a statistically reliable increase in rate of glomerular filtration only after intake of scopolamine combined with levopa, although when each of these agents was taken separately there was only insignificant difference in glomerular filtration from parameters obtained with intake of placebo.

After intake of scopolamine, ephedrine or eskuzan, as well as a combination of stugeron and eskuzan, we observed a statistically reliable decrease in potassium excretion in urine, as compared to the control. Since this was not associated with any appreciable change in sodium excretion, or else it decreased to a lesser extent (with intake of eskuzan), there was considerable rise of sodium/potassium coefficient in these cases. After intake of scopolamine and ephedrine, as well as after eskuzan, we observed a decline of natriuresis (see Table). Urea excretion in urine did not change appreciable or consistently in any of the series of studies, as compared to the control, and constituted an average of 29.8±2.7 mg/min.

Electrolyte and creatinine levels in blood serum taken at different stages of AOH (every 1-2 h), as well as before and after hypokinesia, remained within the physiological range with intake of either individual pharmacological agents or combinations thereof, and they did not differ from control levels demonstrated during AOH after intake of placebo.

Thus, the pharmacological agents we used, according to subjective assessment, alleviated and accelerated man's adaptation to AOH, and this preventive, protective effect did not result from the effect of the tested agents on fluid-electrolyte metabolism. However, individual pharmacological agents could affect excretion of electrolytes in urine by altering their transport in the renal tubules, since glomerular filtration did not change in most cases. This must be taken into consideration when prescribing such agents, particularly in cases where the main factor (for example, circulatory insufficiency, edema syndrome or gravity factors) specifically affects fluid-electrolyte metabolism and renal function.

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LETTERS TO THE EDITOR

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DOES DANDY SYMPTOM OCCUR IN WEIGHTLESSNESS?

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 17, No 1, Jan-Feb 83 (manuscript received 18 May 82) pp 94-95

[Article by G. I. Gorgiladze]

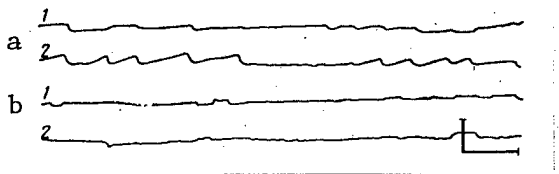
[Text] Individuals suffering Meniere's disease and submitted to bilateral transection of the vestibular nerve develop illusions of movement of surrounding objects when they move their head. This phenomenon was first observed and described by Dandy [1]. Subsequently this phenomenon was confirmed by a number of researchers and was named the Dandy symptom: with elimination of function of one or both labyrinths as a result of surgical intervention or under the effect of large doses of streptomycin, when patients moved their head, walked or ran, they developed the illusion of movement of objects around them (displacement, "floating" away, rocking, vagueness of outlines) and reported diminished visual acuity. They developed considerable difficulties in reading signs, recognizing familiar faces, etc. At the same time, when in a calm state, these signs were usually absent [2-8].

Substantial disturbances of saccadic and compensatory eye movements when fixing the gaze on visual objects in space were observed in studies of primates, submitted to bilateral labyrinthectomy, as well as humans suffering from congenital underdevelopment of labyrinths or submitted, for therapeutic purposes, to surgical destruction of the stricken labyrinth [9-13]. In healthy people, such signs were observed with delivery of vestibular stimuli under laboratory conditions [14]. These oculomotor reactions are among the main elements of gaze fixation, and their coordination with head movements is implemented primarily by vestibular input and, to some extent, proprioceptive input [9, 13].

Visual disorders similar to those described above have also occurred both in weightlessness and in the recovery period. Many Soviet cosmonauts have reported illusions of moving objects when they were in weightlessness, particularly when physically active [15]. According to the report of cosmonaut G. T. Beregovoy, during abrupt turns of the head he had difficulty in "focusing" on objects and "capturing an object in his gaze." Considerable visual disorders in the form of illusions of motion, enlargement, vagueness of outline, distortion of visual objects or their parts and diminished visual acuity have been described during flights in a Kepler parabola [16]. Disturbances referable to coordination of eye movements ("floating" and nistagmoid

movements), increased oculomotor activity and change in position of the eye in the orbit [17, 18] were demonstrated upon recording the electrooculogram on crew members of the Vostok and Voskhod spacecraft, as well as individuals in a brief state of weightlessness during flights in the trajectory of a Keplerian parabola.

V. P. Savinykh, flight engineer aboard the Soyuz T-4--Salyut-6 orbital complex reported that stationary objects appeared to be vague and floated away in the visual field after completion of a 75-day orbital flight, when he moved his head. He also presented distinct impairment of tracking eye movements in response to optokinetic stimulation, whereas spontaneous nystagmus was demonstrated in the dark (Figure).



Spontaneous nystagmus in flight engineer of Soyuz T-4--Salyut-6 orbital complex in the dark, in supine position, with the eyes open 70 min after 75-day orbital flight (a) and absence of nystagmus on 56th day after (b) flight
1, 2) electrooculogram in vertical and horizontal leads, respectively.
Calibration 20°, 1 s

Microelectrophysiological studies of solitary nerve fibers from the frog's vestibular nerve revealed that the transition to weightlessness was associated with marked and prolonged change in otolith afferentation [19]. The change in pattern of signals from labyrinthine receptors and corresponding brain centers inherent in terrestrial conditions probably causes impairment of existing mechanisms of optovestibular interaction. This is manifested by appearance of discoordination between head movements and compensatory eye movements, which leads to shifting of the image on the retina and, consequently, appearance of seeming movement of objects, diminished visual acuity and other signs described under the name of Dandy's symptom.

Adaptation to weightlessness implies development in the central nervous system of a new "nerve model" of optovestibular interaction, which provides for adequate expression of altered afferentation under unusual living conditions. For this reason, subsequent readaptation to earth's gravity could again lead to visual disorders.

The main prerequisite for normal operator work by cosmonauts is retention of stable visual perception during performance of specific actions related to various types of head movements or movement of the entire body, which require proper gaze fixation. For this reason, there is a need to conduct special studies to determine the extent of impairment of this reaction and the range of its adaptive changes in weightlessness and the recovery period. To solve this problem, it is apparently expedient to use the method developed by A. A. Repin [13], which permits recording each component of the gaze-fixation reaction: saccadic movements, turns of the head and compensatory eye movements. In addition, it is necessary to test visual acuity (using the standard table of Sivtsev) at rest and during various head movements (rocking, rotation) or movements of the entire body (rocking, running, etc.), as well as to assess the nature of perception of stationary images of various geometric figures.

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BOOK REVIEWS

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REVIEW OF BOOK ON CLINICAL BIOMECHANICS OF THE SPINE

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[Review by V. S. Kazeykin of book "Clinical Biomechanics of the Spine," by A. A. White and M. M. Panjab, Philadelphia-Toronto, 1978, 534 pages]

[Text] This monograph deals with the structure and function of the human spine. Investigation of biomechanics of the supporting skeleton under normal physiological conditions, as well as in the presence of disease and trauma, is important to comprehension of processes that occur in the human body under the effect of removal of weight from the skeleton under hypodynamic and weightless conditions, as well as under the effect of dynamic factors of air and space flights (vibration, impact accelerations). A unified approach to the study of mechanisms of vertebral injuries became possible thanks to the joint work of a clinical surgeon and engineer. This monograph is one of the largest publications in the worldwide scientific literature dealing with physiology and pathology of the spine. It contains factual material collected in the course of the studies of the authors, and they also generalize data from numerous literature sources.

The book consists of an introduction, eight chapters, conclusion and appendix. There are a bibliography, author and subject indexes after each chapter.

It is noted in the foreword that the monograph is the first book, in which current information is given, not only about the individual segments of the spine, but its function as a whole. The prolonged joint work of the authors has brought them broad international fame among orthopedic surgeons and specialists in disciplines that are on the boundaries of several sciences.

The introduction defines clinical biomechanics of the spine as a science dealing with the human body, in which mechanical facts, conceptions, principles, terms and mathematical theses are used to analyze normal and pathological anatomy and physiology of man for the purpose of determining the state of the spine. There is discussion of causes for the interest of physicians and engineers, which has heightened in recent years, in the study of biomechanics of the spine. The timeliness of the book is validated; its goals and tasks are formulated; a brief description is offered of different parts.

Chapter 1 submits information about the physical properties and functional biomechanics of the spine. It starts with consideration of the structure of

individual intervertebral disks, ligaments, vertebrae, ribs and muscles of the spine. Comprehensive light is shed on questions of correlation between physical properties and function of individual elements. Information about anatomy and physiology is well-combined with data referable to mechanical tests. All of the technical terminology is explained in detail using examples and illustrations. Of special interest is the section dealing with mathematical modeling of spinal reactions to exogenous factors, including vibration and impact accelerations.

Chapter 2 submits data about the kinematics of the spine, the relevant terminology is explained, and the link between movement and activity of spinal muscles is demonstrated. A detailed analysis is made of kinematics of the cervical, thoracic and lumbar regions of the spine; their anatomical structure and range of motion are compared. The effect of age and sex is described, and the link between diseases and spinal kinematics is discussed.

The third chapter deals with practical application of knowledge about biomechanics to the study of etiology, pathogenesis and clinical manifestation of scoliosis. Methods are described for studying and treating curvature of the spine.

The fourth chapter is of direct relevance to the practice of aerospace medicine. It analyzes biomechanical aspects of spinal trauma, discloses the principal mechanisms of such trauma, and the authors' own clinical cases are submitted. On their basis, an original classification is proposed for injuries to the spine. In the conclusion, a survey is made of specific lesions to the cervical, thoracic and lumbar regions of the spine.

Chapter 5 discusses the main problems related to clinical instability of the different elements of the spinal column. This chapter consists of an introduction and five parts, which systematically discuss anatomical distinctions and biomechanical factors that lead to functional impairment in the cervical, thoracic, lumbar regions of the spine and sacrum. Recommendations are offered for diagnosing and correcting these disturbances.

The sixth chapter deals with clinical biomechanics of pain in the spinal column. The authors discuss etiology, diagnosis, treatment and prevention of such disorders.

The ergonomic recommendations, which were made on the basis of a comprehensive study of correlation between different elements of the spine in different working positions, merit special attention.

The seventh and eighth chapters discuss questions related to correction of spinal disturbances by palliative and surgical methods.

The appendix merits special attention; in it, the authors discuss in an understandable way the terms most frequently used in clinical biomechanics, and they cite examples that illustrate their meaning and area of application.

The book is well-illustrated with figures, photographs, charts and diagrams.

This monograph, which is intended for a wide circle of physicians working in the field of physiology and pathology of the locomotor system, will

definitely be of great interest to specialists in aviation and space medicine who are concerned with development of means of protection against impact accelerations and prevention of the adverse effect of weightlessness on the skeletomuscular system.

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